THERAPEUTICS OF THE CIRCULATION

BRUNTON

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THERAPEUTICS OF THE CIRCULATION

BY SIR LAUDER BRUNTON, Bt.

M.D., D.Sc., LL.D. (Edin.), LL.D. (Aberd.), F.R.C.P., F.R.S.

CONSULTING PHYSICIAN TO ST BARTHOLOMEW'S HOSPITAL

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PREFACE

THE first edition of this book consisted of eight lectures delivered in the spring of 1905, at the request of Professor Waller, in the Physiological Laboratory of the University of London, and published under the auspices of the University. The purpose of such lectures, as expressed by the University in establishing them, was "to present the results of recent investigations by the investigators themselves." For this reason my own work on the circulation occupied a part which would have been unduly prominent in an ordinary textbook. The lectures were illustrated by experiments, and it was sometimes necessary to adapt the lectures to the experiments, so that the sequence of subjects was not so orderly as it would otherwise have been. In preparing a second edition I have tried to avoid both of these faults, and have made many alterations and additions, with the object of increasing the practical utility of the book. The arrangement of subjects has been altered, the matter divided for greater convenience into chapters, and so much new matter added that the book has practically been rewritten. Delay in its appearance is due to the fact that pressure of other work has pre-

vented me from writing, except during autumn holidays, so that an interval of more than ten months occurred between writing the first and second parts, and a similar one between the second and third parts. When the lectures were first given in 1905 the measurement of blood-pressure was by no means common in this country, and a full description of the instruments used to measure it was given. It is now so commonly employed that most of these instruments have been omitted. On the other hand, recording the venous pulse and electrical examination of the heart have now become established as practically important, and a short account has been given of these methods. This book is not intended to replace, but only to supplement the usual text-books dealing with the circulation. Much space is therefore devoted to physiology, to pharmacology, and to the pathology of living structures as forming a basis for scientific therapeutics, but morbid anatomy and diagnosis, which are usually dealt with at great length in text-books on the heart and circulation, are barely mentioned here.

I may, perhaps, be allowed to forestall the very obvious criticism that this book contains much physiology, pathology, and pharmacology in proportion to actual therapeutics by pointing out that the keystone of a bridge, which makes it passable, is quickly placed in position, but it takes a long time to build the piers on which it must rest; and that a surgeon may only take a few minutes to perform an operation, but needs years to learn his anatomy so thoroughly that

he can guide his knife swiftly and surely to a successful result.

In preparing this edition I have consulted books and papers by Cushny, Dixon, Gaskell, Gottlieb, Huchard, Langley, Lewis, Mackenzie, Osler, Schmiedeberg, Waller, and others too numerous to mention; but I have received special help from the treatises of Gibson and of Hirschfelder on *Diseases of the Heart and Aorta;* from Kraus and Nicolai's work, *Das Electro-Cardiogram;* from Meyer and Gottlieb's, *Experimentelle Pharmacologie*, and from Tigerstedt's admirable *Lehrbuch der Physiologie des Kreislaufs.* I have also to thank my friend Professor Kronecker most heartily for his kindly criticism and help, and to express my very great obligation to Dr W. J. Dilling, who has not only revised and corrected all the proofs of the book, but has verified the references in the literature of the first fifteen chapters and himself supplied all the references to subsequent chapters.

Although I had myself verified almost every reference in the first fifteen chapters, by reference to the original work or paper, yet in copying my manuscript so many errors had crept in that the literature would have been untrustworthy, whilst now I believe it is correct, and will be a great help to every one who wishes further information in regard to any statement made or subject mentioned in this book.

TO

HUGO KRONECKER

M.D., D.Sc. (CANT.), LL.D. (ABERD. AND GLASG.)

ETC., ETC.

PROFESSOR OF PHYSIOLOGY IN BERNE, LATE DIRECTOR OF THE MAREY INSTITUTE IN PARIS

THE AUTHOR DEDICATES THIS BOOK

IN ACKNOWLEDGMENT OF THE GREAT SERVICES HE HAS RENDERED TO PHYSIOLOGY, AND ESPECIALLY TO THE PHYSIOLOGY OF THE CIRCULATION; IN MEMORY OF MANY PLESAANT HOURS SPENT TOGETHER WHEN WORKING IN LEIPZIG UNDER THE DIRECTION OF THEIR BELOVED MASTER, CARL LUDWIG, IN 1869-70, AND IN TOKEN OF A FRIENDSHIP THAT HAS LASTED EVER SINCE.

CONTENTS

CHAPTER I

GENERAL PHYSIOLOGY OF THE CIRCULATION

CHAPTER II

PHYSIOLOGY OF THE HEART

CHAPTER III

PHYSIOLOGY OF THE MAMMALIAN HEART

CHAPTER IV

PHYSIOLOGY OF VESSELS: BLOOD-PRESSURE

CHAPTER V

EXAMINATION OF BLOOD-PRESSURE IN MAN

CHAPTER VIII

SYMPTOMS OF DISORDERED CIRCULATION

CHAPTER IX

ORGANIC DISEASES OF THE HEART

CHAPTER X

METHODS OF TREATMENT IN CARDIAC DISEASE

CHAPTER XI

ACTION OF CARDIAC AND VASCULAR REMEDIES

CHAPTER XII

ACTION OF CARDIAC TONICS

CHAPTER XIII

ACTION OF CARDIAC DEPRESSANTS

CHAPTER XIV

ACTION OF DRUGS ON BLOOD-VESSELS

CHAPTER XV

ACTION OF DRUGS ON THE URINARY, DIGESTIVE, AND NERVOUS SYSTEMS

CHAPTER XVI

TREATMENT OF ACUTE HEART DISEASE AND OF CONVALESCENCE

CHAPTER XVII

GENERAL PRINCIPLES OF TREATMENT IN HEART DISEASE

LIST OF ILLUSTRATIONS

THERAPEUTICS OF THE CIRCULATION

CHAPTER I

GENERAL PHYSIOLOGY OF THE CIRCULATION

Introduction—Harvey's Discovery—The Heart—Sleep of the Heart—The Arteries—Motor and Peristaltic Action of the Arterioles—Lister's Observations—Capillaries and Veins—Self-massage of Arteries—Action of Fasciæ—Accessory Muscles of Circulation—Lymph and Blood—Flow of Lymph—Arterial Tension or Blood-pressure—Estimation of Blood-pressure—Regulation of Blood-pressure—Co-ordination of Heart and Blood-pressure—Arteries and Blood-pressure—Influence of the Muscular Area—Influence of the Splanchnic Area—Distension of Liver—Cutaneous Area—Cerebral Area—Depressor Nerves—Independent Pulsation of the Vena Cava and Pulmonary Veins.

THE subject of these lectures is "The Therapeutics of the Circulation": the means by which we can put right anything that may have gone wrong with the circulation. If I were to hand my watch to any one of you and tell you it was not going properly, you would naturally hand it back to me and tell me to take it to a watch-

maker; because you know nothing of the way in which watches are built, of the disorders to which they are liable, or the way in which to put them right. In the same way, before you can put anything right which has gone wrong with the circulation, you must know something about—

(1) Its normal working, or physiology;

(2) The disorders to which it is liable, or pathology;

(3) The means by which we can act upon it, or pharmacology;

(4) The indications by which we recognise the particular disorder, or semeiology; and

(5) The methods of applying our remedies to the disorders which we have already recognised, or therapeutics.

It is evident that, before we can deal with therapeutics satisfactorily, we must take up, to a certain extent, the other subjects upon which it depends; and although you have studied them all to a certain extent already, I think it will be advisable to go shortly over them, more especially as I shall have to take them in definite relation to their practical use, instead of merely considering them as scientific subjects unconnected, possibly, with practical medicine. But the treatment of these must necessarily be very brief, because the subject-matter to be considered is very great.

Harvey's Discovery.—There is, perhaps, no discovery, either ancient or modern, which has had such a far-reaching influence on the health of human beings as the discovery of the circula-

tion by Harvey. The truth of this discovery was at first denied, then its importance was belittled, then it was attributed to other men; but now its full importance is recognised, and the claims of Harvey to the discovery acknowledged. When we look at Harvey's work, it seems almost incredible that for so many thousands of years men should have overlooked the circulation. When we read Harvey's own account of his discovery, it seems one of such amazing simplicity that one is inclined to think that nobody could have helped making it. In his own words, it occurred to him "whether there might not be a motion (of the blood), as it were, in a circle."[1] That it did go round, Harvey showed by the blood issuing from the proximal end of a cut artery, and by the swelling of the veins when an obstruction was put between the periphery and the centre.

One of the great reasons why the blood had been supposed not to go round, but to flow backwards and forwards, probably was that the ancients looked upon the arteries as conveying air alone instead of blood, or else conveying a mixture of air and blood. They seem to have come to this conclusion from the fact that the arteries were generally found empty in animals that had been killed for sacrifice; and the reason of their emptiness I shall discuss later, on p. 8.

Physiology of the Circulation.

The Heart.—The great motor power which

keeps the blood moving in a circle is the heart, although its action is supplemented by other mechanisms in the vessels and tissues. We are sometimes accustomed to speak of this "unresting" organ, but this is a total mistake. The heart rests in an adult more than thirteen hours out of the twenty-four; the time of rest being the diastole, and the time of work being the systole. With a pulse of 70, Edgren determined the duration of the systole to be 0·379 seconds, and of the diastole 0·483 seconds (Schäfer's *Textbook of Physiology*, vol. ii., p. 38). The duration of the cardiac cycle is thus $0{\cdot}379 + 0{\cdot}483 = 0{\cdot}862$ seconds, and the time occupied in diastole in twenty-four hours is therefore 0·862 : 0·483 : : 24 : 13·44—*i.e.*, more than thirteen hours. In his introduction to *Human Physiology* (p. 52), Waller gives the normal work of the heart as nine hours, and the rest as fifteen hours daily. In his Oliver-Sharpey Lectures of 1913 he* considers that the heart which works at this rate is ordinary, that one which works eight hours is very good, and that one which is working over twelve hours a day is in a bad condition.

Sleep of the Heart.—We may say, then, that the heart practically sleeps more than the brain or the body; but the great distinction between the sleep of the heart and that of the brain, is that the sleep is so short at a time. There are very few healthy men who could not walk a thousand miles in six weeks, walking a little over eight hours a day at an easy pace, and resting for the remainder of the period; but

* *Lancet*, 1913, vol. i., p. 1520.

there are not many men who could emulate the feat of Captain Barclay, of walking a thousand miles in a thousand hours, because the frequent interruptions to their sleep would exhaust them completely ; and still fewer are there who could walk a thousand miles in a thousand half-hours, as has been done by various men since Captain Barclay's time. In such trials of endurance a man usually walks two miles at a time, the first mile at the end of one hour or half-hour, and the second at the beginning of the next hour or half-hour. Supposing he walks at the rate of four miles an hour—*i.e.* a mile in a quarter of an hour—he gets an hour and a half for sleep between every walk when doing a thousand miles in a thousand hours, but only gets one-third as much sleep, viz., half an hour, between his walks when doing this distance in a thousand half-hours. An attempt to do a thousand miles in a thousand quarter-hours is obviously impossible ; if a man walked at the rate of four miles an hour there would be no time for rest at all, the whole time being required for walking. A little time might, no doubt, be gained by increasing the pace; but this would of itself involve greater exertion, and the time thus gained would be quite insufficient for recuperation.

In the same way, when the heart is forced to beat more quickly than normal, it becomes more and more quickly exhausted the higher the pulse-rate rises, because nearly the whole time for the extra work is taken from the diastolic pauses or sleep of the heart, even though the systole may be slightly shortened. Hence

the importance of slowing the pulse-rate by rest, by cold, by drugs, or by other measures, when it tends to become too rapid.

Perhaps it may be as well here that I should note that the heart, at certain periods, is resistant to external stimuli. When Captain Barclay was taking his sleep between his walks, he would be more and more ready to respond to a chance call the nearer the time came for him to begin again ; but while actually engaged in his walk, he would be too much intent upon his work to heed a call from anyone. In the same way, we find that during the period that the heart is contracting it will not respond to a stimulus which, if applied immediately after its action is over, would cause it to contract again. This period, which we have to consider later on, is called the refractory period.

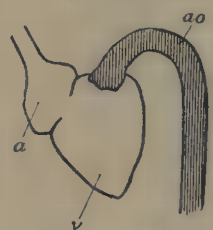


FIG. 1.—Diagram to show how the blood under pressure in the aorta is shut off from the rest of the heart during diastole by closure of the sigmoid valves. *a*, Auricle ; *ao*, aorta ; *v*, ventricle.

The Arteries: their Triple Function.—Now, if the heart is only acting for eleven hours out of the twenty-four, and is entirely cut off from the aorta by the closed aortic valves (Fig. 1), what force is carrying on the circulation during the

whole of the other thirteen? This force is the elastic recoil of the arteries, which have been stretched by the blood forced into them during the ventricular systole, but which, if healthy, again contract during the diastole. The vessels thus act as a storage of energy; just like a watch-spring when wound up every night, or like the water driven by a force-pump into a high tank from which a house or town can be supplied, or like the elastic bag in a spray-producer.

The arteries have really three functions. They not only act as (1) storers of force, as just mentioned, but as (2) regulators, and as (3) motors.

Storage Action.—This is chiefly effected by the aorta and larger arteries, which contain a quantity of elastic tissue.

Regulating Action.—Their power of regulating the supply of blood to different parts of the body was known to Harvey, who said: "It is manifest that the blood in its course does not everywhere pass with the same celerity, neither with the same force, in all places, and at all times. . . . In fear, and under a sense of infamy and of shame, the face is pale; but the ears burn, as if for the evil they heard or were to hear."[2] As my old teacher, Professor Ludwig, used to put it, "There is not nearly sufficient blood in the body to fill all the vessels at once, and the vaso-motor system, which regulates the size of the arteries, is like the turncock in a large town who turns off the water-supply to one district at the same time that he turns it on to another"; just as in Harvey's observation,

the vessels became contracted in the face at the same time as they became dilated in the ear. All organs when functionally active require a larger supply of blood than they do when quiescent, and when they act the arteries supplying them dilate so as to allow a larger supply of blood to flow to them; when their action has ceased, the arteries again contract.

Motor and Peristaltic Action of Arteries.—The motor action of the arteries has received less attention; but it is, I think, very important, and is, I believe, the cause of the emptiness of the arteries after death, which so long prevented Harvey's discovery from being made. When working under Professor Ludwig in 1869, he directed my attention to the contractile power of the arterioles apart from any nerve centre, and while watching their movements I have sometimes seen a regular peristaltic action take place, by which the blood was driven forward in the arteriole, just as fæcal matter would be driven forward in the intestine.[3] Such action may empty the arterial system after death (p. 3).

Lister's Observations.—Since these lectures were given I have found that similar observations had been previously made by Lord Lister, who records that in the amputated limb of a frog the artery "was sometimes constricted to absolute closure in one part of its course, and dilated to a very considerable degree—*e.g.* $3\frac{1}{2}°$—in another part. More commonly, however, the artery, though never uniform in size as in health, had a general tendency either to moderate constriction or dilatation. The varia-

tions occurred frequently during the twenty-four hours, and on one occasion I saw the artery in the act of slow contraction at one part driving the blood into a dilated portion at a little distance."[4]

Capillaries and Veins.—From the arteries the blood passes into the capillaries, and some of its liquid parts, with a few white corpuscles, leak through their walls to supply the needs of the tissues, while the remainder, along with the red corpuscles, passes into the veins.

Flow of Blood in the Veins.—As Kronecker points out, the hydrostatic pressure in the vascular system tends to make the blood in the veins rise to the same height as in the arteries, in the same way as mercury stands at the same level in the two limbs of a U-tube. This makes it possible for the blood in the veins of a man standing upright to rise from the feet up to the heart, a distance of more than 3 feet, while the actual impulse which the blood in the vena inferior receives from that of the aorta is about 5 millimetres. It is evident that this impulse would be barely sufficient to carry on the circulation and bring the blood back to the heart again, were it not for various helping agencies.

Assistant Factors in the Circulation.—One of these is the suction exerted by the movements of inspiration, and another is the suction exerted by the heart itself during the ventricular contraction, which at the same time that it drives the blood out of the thorax, and through the aorta, sucks it in from the great veins (p. 154).

One very important adjunct to the heart in keeping up the venous circulation, is intermittent pressure upon the veins from without, aided by numerous valves in the veins themselves; so that while each pressure pushes the blood a little onwards, its return is prevented. External pressure is produced by muscular action. Each contraction of a muscle squeezes the blood and also the lymph out into the veins and lymphatics, both of which have very numerous valves at short distances apart. But every beat of the arteries, as a rule, tends also to help on the venous blood, for the arteries and veins usually have a common sheath of unyielding fibrous tissue (Fig. 2, *a*), and each

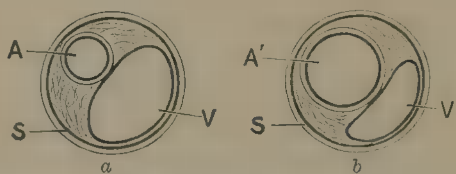


FIG. 2.—Diagram to show the effect of the arterial pulse in aiding the onward flow of venous blood and lymph, by a process of what may be called self-massage. A is an artery during diastole. V is a vein filled with blood. S is the fibrous sheath which encloses the artery, the vein, and the lymph space around them. A′ is the artery distended with blood by the ventricular systole. As the sheath S′ is unyielding, the distension of the artery forces the blood out of the vein and the lymph out of the lymph space, and as the backward flow of both is prevented by the valves of the veins and lymphatics, the circulation is increased in both.

time that the artery is distended during a ventricular systole it tends to push a corresponding amount of blood onwards through its accompanying vein (Fig. 2, *b*).

Self-Massage of Arteries.—At the same time the vasa vasorum of the artery itself are

affected in a similar manner, and each pulsation of the heart constitutes a kind of gymnastics of the arteries, and tends to preserve their cohesion, elasticity, and contractility.

In Ludwig's first experiments with artificial circulation he employed blood under constant pressure, but found that as the experiment went on the pressure required became greater and greater, and the tissues tended to become œdematous. Hamel, under Kronecker's direction, found that more blood can be driven through the vessels in a given time by filling them rhythmically than by passing a stream through them under constant pressure. They also retain their healthy properties, and œdema does not occur.[5]

Action of Fasciæ.—In addition to these mechanisms, however, we have the pressure exerted upon the veins by the fasciæ of the limbs, and Braune has shown that when the veins are stretched, their capacity is increased, and they suck blood into them. The veins of the upper limbs are most stretched when the fists are clenched, the hands bent somewhat down, and the arms extended and pushed rather backwards—the very attitude, indeed, that is assumed by a man who has been sitting for a length of time at a writing-table and feels himself cramped in consequence. The veins become relaxed when the leg is bent and turned slightly inwards, whilst the veins become stretched when the foot is turned outwards and the leg extended and pushed somewhat backward. The first of these positions is nearly that

assumed by one leg when we advance it for the purpose of walking, and the second when we move the body and other leg forward.[6]

Accessory Muscles of Circulation. — The late Professor Sharpey used to insist a good deal upon the functions of the rotators of the leg, and he pointed out that in books on anatomy the trunk is looked upon as a fixed point, and the rotation is discussed in terms of this; so that we say that the function of the tensor vaginæ femoris is to rotate the leg inwards upon the body, and that of the gluteus maximus to rotate it outwards. In reality, he said, when the foot is planted on the ground it is the leg which is the fixed point in walking; and the function of these muscles is to rotate the body on the leg, the tensor vaginæ femoris rotating, not the leg inwards, but the body outwards, so as to bring the centre of gravity over the foot. But in view of Braune's observations these muscles acquire a new value. We speak very frequently of accessory muscles of respiration, but I have not seen anywhere the tensor vaginæ femoris and the gluteus maximus spoken of as accessory muscles of circulation, yet both they and the muscles of the calf and thigh may well deserve such an appellation.

Lymph and Blood. — The old expression, "The Blood is the Life," is true to a certain extent, for when the circulation of the blood ceases the body dies; and if blood be kept circulating artificially in any part of the body, it may be kept alive for hours or even days

after the rest of the body is dead (*Ueberlebende Organe*, of Ludwig).

And yet blood itself is an irritant, and when brought into immediate contact with the substance of muscles and nervous ganglia, it injures them.[7] It is the tissue-juice or lymph which nourishes the tissues, and in it they live. As Claude Bernard has well put it, we live in a fluid internal medium.[8] A fish swimming in water is not living in air although the glass globe in which the water is contained may be standing on a table surrounded on all sides by air, and although our bodies as a whole are surrounded by air, our tissues live in the intercellular fluid in which they are bathed, in the same way as a fish lives in the water. But just as the water requires to be aerated and food supplied to the fish, so the lymph requires oxygen and nutriment, and these it receives constantly from the blood in the capillaries. Some of the waste products of tissue metabolism probably return to the capillaries, and some are carried back in the lymph into the general circulation.

One of the most important of all the waste products is CO_2, which acts as a poison to the tissues, and must be constantly removed from them. Its removal is effected by the alkaline salts in the serum. All tissues and animals are not equally affected by CO_2; for, according to Kronecker, goldfish live for a whole day in water that has been boiled, then cooled, placed in a bottle and hermetically sealed, while brook trout die in a few minutes; and many people

require a constant fresh supply of fresh air, while others are perfectly comfortable in small, close rooms.

Flow of Lymph.—It is evident that any description of the circulation would be insufficient without a consideration of how the lymph flows, for the circulation of the lymph is quite as necessary as that of the blood itself. Here also the muscles form one of the most efficient sources of motor power. At each relaxation of a muscle it tends to cause a vacuum within its surrounding fascia, into which the lymph flows from the muscular structure.[9] At each contraction the muscle presses this lymph out, and these alternating muscular movements really act as a subsidiary heart, and do away with the necessity of having in mammals the lymph hearts which are seen in the frog.

In the pleura and the diaphragm the movements of respiration have a similar pumping action on the pleural and peritoneal fluids.[10]

It may seem that I am spending too much time upon points in the circulation which you all know, but I shall have to return to them again in discussing Treatment, and unless I had put them before you now in the way I have done, you might not be so readily able to perceive the reason for the therapeutic measures which I shall afterwards have to mention.

Arterial Tension or Blood-pressure.—During the long sleep of the heart—thirteen hours out of every twenty-four—the circulation is maintained by the contractile force of the arteries,

which presses the blood out through the only opening which, in health, is available, namely, through the capillaries. This contractile power is, of course, to a great extent, due to elasticity, especially in the larger arteries, although in the arterioles it is probably chiefly due to contractility. The force with which the blood would be pressed out if a vessel were opened or a cannula put into it, is known as the blood-pressure.

Estimation of Blood-pressure.—It is usually estimated by connecting an artery with a mercurial manometer, and seeing the height of mercury required to counterbalance the pressure in the vessels. It was first estimated by a clergyman, the Rev. Stephen Hales,[11] who after cutting an artery in an animal, and connecting a glass tube with the artery, noted the height to which the blood rose in the tube. Poiseuille[12] improved upon this plan, by connecting the artery with a mercurial manometer; and an immense advance was made by Ludwig,[13] who registered the movements of a mercurial manometer on a revolving cylinder. To this recording manometer he gave the name of kymograph (Fig. 3, p. 16).

Although he did this in 1847, yet in 1865, when I first began to work at the action of drugs on the blood-pressure, there was, I believe, not a single recording manometer in this country,[14] and it was only at this time that one was first made by Sir John Burdon-Sanderson,[15] and used by him in his research upon the relationship of respiration to circulation. It

was just a little before this that Marey[16] invented his sphygmograph, by which much interesting information has been gained regarding the circulation in man.

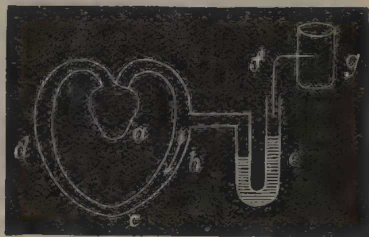


FIG. 3.—Diagram of the circulation. *a*, The heart completely shut off by the valves during diastole from *b*, the arteries; *c*, the capillaries; *d*, the veins; *e*, mercurial manometer; *f*, a float; *g*, a recording cylinder.

Regulation of Blood-pressure.—The blood-pressure, one may roughly say, depends upon the difference between two factors, viz., (1) the amount of blood pumped by the heart into the cardiac end of the arterial system in any given time, and (2) the amount running out of the arterial system at the other end through the capillaries into the veins in the same time. It is obvious that unless some means existed by which these two factors could be brought into proper relationship, much mischief might be done.

If the heart were to continue pumping in blood whilst the arterioles were tightly contracted, the pressure would rise so high that either a vessel would burst, as it does in apoplexy, or the heart would be strained; or, as Waller has shown, the left auricle might stop altogether.[17] On the other hand, if the

arterioles were dilated and the heart did not beat more actively, so as to supply a larger amount of blood, the arteries would become so empty and the pressure in them so low that the circulation through the various organs would be insufficient to maintain their functional activity; and the brain, being especially sensitive, syncope would result.

Co-ordination of Heart's Action and Blood-pressure. Centres in Medulla Oblongata.—Co-ordination is maintained by means of the nervous system, the chief centre of which is in the medulla oblongata, where the most important part of the vaso-motor centre is located, and where also the vagus roots are situated. By irritation (*a*) of the vagus roots, or (*b*) of their trunks, or (*c*) of their ends in the heart, the movements of the heart become slower and often weaker; although the slowing and weakness may occur more or less independently of each other. Any excessive tension in the vessels, involving as it does the blood-supply of the medulla, acts as an irritant to the vagus centre, puts the vagus nerve into action, slows the heart, and thus prevents the tension from rising too high.* On the other hand, diminished pressure in the arterial system lessens the normal stimulation of the vagus centre, so that the vagus nerves act less powerfully on the

* François Franck (*Traveaux du laboratoire de Marey*, 1877, vol. iii., p. 276) has shown this in a brain kept alive by artificial circulation and separated from the rest of the body, except that the vagi remained intact, so that the brain could act on the heart.

heart, its beats become quicker, and the pressure rises.

Arteries and Blood-pressure.—On the other hand, the vaso-motor centre, when in action, causes the arterioles, especially of the intestines and of the skin, to contract, so that the channels by which the blood can pour from the arteries into the veins are diminished in size, and the pressure, consequently, tends to rise.

Effect of Anæmia and Suffocation. — All centres in the medulla oblongata are excited by anæmia; the vagus roots, the accelerating centre, the vaso-motor centre, and also the convulsant centres, are excited by anæmia and suffocation; but in such conditions the inhibitory is greater than the accelerating action, so that the pulse in asphyxia tends to become slow.

Influence of the Muscular Area.—All arteries do not contract equally when the cervical cord is stimulated, and there are a number of arteries which are only slightly influenced by the vaso-motor centre, for, when this centre is irritated so as to contract all the vessels of the skin and intestines to the utmost, blood may still pour through those vessels which supply the muscles so rapidly that the effect of the vaso-motor centre hardly appears to be felt at all.[18] Nevertheless, Waller noticed that sometimes by stimulating this centre the tension may rise so high as to prevent the left auricle from beating; although Ewald has found that the left ventricle of a dog is capable of overcoming four times the normal pressure.[19] These different results depend, of course, upon the different animals experimented

upon and the different conditions under which the experiments are made. The reserve power of the healthy ventricle is most important, and is in marked contrast to its condition in disease.

Influence of the Splanchnic Area.—The four largest vascular districts in the body are those of (1) the splanchnic area, (2) the muscles, (3) the brain, and (4) the skin. It is the splanchnic area which is more especially under the influence of the vaso-motor centre. Any disturbance of the circulation in this area greatly modifies the blood-pressure, and section of the splanchnic nerves will reduce it enormously. The splanchnic area, therefore, serves to a great extent as a regulator of blood-pressure; and when the portal system is dilated by ligature of the portal vein and aorta [20] the whole of the blood in the body, or at least a large part of it, will collect in the vessels of the intestines and in the liver; so that, to use Ludwig's words, "an animal may be bled into its own veins." This occurs in sudden death, so that the arteries are empty (*vide* pp. 3, 8).

Distension of Liver.—In the healthy body we do not notice great changes in the liver, because the pressure in the portal system undergoes but very slight alteration. However, when there is backward pressure from the heart, in consequence of incompetency of the tricuspid valves, the liver sometimes becomes enormously large, reaching down to the umbilicus, or even to the iliac fossa, and may again become smaller when the venous pressure is relieved.

In 1868 Ludwig [21] and one of his pupils made

some experiments upon the secretion of bile by an excised liver, through which a stream of blood was passed artificially; and on making experiments myself a year or two later,[22] I was very much struck by the enormous distensibility of the liver. One is misled in regard to this property by the hard, firm appearance of the liver after death; but during life the liver is more like a sponge, and reacts just like a sponge to the slightest difference in blood-pressure, swelling up as the pressure increases, and diminishing as the pressure falls.

Cutaneous Area.—Harvey's observations (p. 7) regarding the colour of the face and ears, show that the cutaneous vessels may contract in one place and dilate in another. As a whole, however, the cutaneous vessels tend to dilate when those of the splanchnic area contract, and *vice versa*. On this account, when the cutaneous vessels are dilated by warmth, the blood is withdrawn from the splanchnic vessels and congestion is relieved, while cold to the skin drives the blood into the intestinal vessels.[23] These actions are not simply due to mechanical displacement of blood from one area to another, but are produced reflexly through the nervous system.[24]

Cerebral Area.—The existence of vaso-motor nerves in the cerebral arteries has been denied, and changes in the cerebral circulation asserted to be simply of a passive nature depending on the general blood-pressure. Nevertheless it is almost certain that the cerebral vessels contract and relax independently of those in other parts of the body, and sometimes, indeed, relax

while others contract, and *vice versa.*[25] Certain drugs which act locally on vessels, such as adrenalin, cause the cerebral vessels to dilate while they cause most other vessels to contract.[26]

By injecting paraffin into the cerebral vessels so as to measure the contents, Kronecker, Marckwald, and Henriques found that the arteries of the brain contained very little blood, no more than one-tenth of a cubic centimetre in rabbits.[27] At the same time the flow of blood through the brain, as shown by the capacity of the carotids and the rate of flow through them, appears to be very considerable.[28]

Depressor Nerves.—As I have already mentioned, when the tension is too great in the heart and aorta, it acts as a stimulus to nerves, starting from the heart and aorta, and causing reflex dilation of the abdominal vessels, so that the tension in the heart is thus relieved. These nerves may either run as a separate nerve, known as the depressor nerve,[29] or may be partly incorporated with the vagus trunk[30] (p. 65).

Independent Pulsation of the Vena Cava and Pulmonary Veins.—All through the venous system the circulation is steady and even, until we come to the vena cava and pulmonary veins, when we find that these vessels may have a pulsatile contraction of their own, like that of the venous sinus in the frog. This action of these veins had apparently been lost sight of until Fayrer and I rediscovered it in 1874, and we could not then find any mention of it in any of the ordinary textbooks on physiology.[31] It

was, however, well known to Meibomius,[32] to Haller,[33] and also to Senac,[34] a century and a half ago, and we have since found it had been noticed by Colin[35] a year or two before our observation. This contraction is not always present, and so it can hardly be regarded as a constant part of the cardiac pulsation. It is possible, however, that in some pathological conditions, such as mitral stenosis, it may become very important.

LITERATURE.

1 Harvey's *Works*, Syd. Soc. Ed. 1847, p. 46.

2 *Ibid.*, pp. 128 and 129.

3 Lauder Brunton, *Sitzungsb. d. k. säch. Gesellsch. d. Wiss.*, 1869, p. 285; *Ludwig's Arbeiten*, 1869, p. 101.

4 Lister, *Report of the Meeting of the British Association, Dublin*, 1857, p. 114. Reprinted in his Collected Papers, vol. i., p. 39 (Oxford: Clarendon Press, 1909). Also M. Schiff, *Arch. f. physiol. Heilk.*, 1854, vol. xiii., p. 527.

5 Hamel, *Ztschr. f. Biol.*, 1889, vol. xxv., p. 474.

6 Braune, *Beiträge z. Anat. u. Physiol. als Festgabe*, Carl Ludwig gewidmet, 1874, p. 5.

7 Kühne, Setschenow und Paschutin, quoted by Hermann, *Handb. d. Physiol.*, 1879, Bd. i., Theil 1, p. 103.

8 Claude Bernard, *Leçons de Pathologie expériment.* p. 439.

9 Generisch, *Ludwig's Arbeiten* for 1870, p. 53.

10 Dybkowsky, *Ludwig's Arbeiten* for 1866, p. 40.

11 Hales, *Statical Essays*, London, 1733, vol. ii., p. 1.

12 Poiseuille, *Magendie's Journ. de la physiol.*, viii., p. 272, 1828; ix., 1829, p. 343.

13 Ludwig, *Arch. f. Anat. u. Physiol.*, 1847, p. 242, Taf. x., xiv.

14 Lauder Brunton, *On Digitalis*, 1868 (London: Churchill); and *Collected Papers on Circulation and*

Respiration, First Series, 1907, pp. 52 and 104 (London: Macmillan & Co.).

15 Burdon-Sanderson, *Roy. Soc. Proc.*, xv., 1867, p. 391; *Phil. Trans.*, clvii., 1867, p. 571.

16 Marey, *Mem. Soc. Biol.*, 1859, p. 281; *Compt. rend.*, 1860, i., p. 634.

17 Waller, *Archiv f. Anat. u. Physiol.*, *physiol. Abtg.*, 1878, p. 525.

18 Ludwig and Thiry, *Sitz. Ber. d. Wien. Akad.*, 1864, vol. xlix., Abt. ii., p. 45; Ludwig and Hafiz, *Ludwig's Arbeiten*, for 1871, p. 106.

19 J. R. Ewald, *Berl. Klin. Woch.*, 1885, p. 834.

20 Ludwig and Thiry, *op. cit.* Claude Bernard, *Leçons sur les propriétés physiol. des liquides de l'organisme*, 1859, tom. i., p. 196; Kronecker and Gautier, *Rév. de Méd.*, Oct. 1911, p. 373.

21 Ludwig and Schmulewitsch, *Ludwig's Arbeiten*, 3ter Jahrg., 1868, p. 114.

22 Lauder Brunton, *Burdon-Sanderson's Handbook for the Physiological Laboratory*, 1873, p. 505 *et seq.*; and Lettsomian Lectures, 1885, in *Disorders of Digestion*, p. 25.

23 Heidenhain, *Pflüger's Archiv*, 1870, vol. iii., p. 504 *et seq.*, and 1872, vol. v., p. 113; Dastre and Morat, *Système nerveux vasomoteur*, Paris, 1884, p. 330; and Bayliss, *Journ. of Physiol.*, 1893, vol. xiv., p. 303 *et seq.*

24 Wertheimer, *Arch. de Physiol.*, 1894, p. 308; Otfried Müller, *Deutsch. Arch. f. klin. Med.*, 1905, 82, p. 574.

25 For discussion of this subject and references to literature, *vide* F. Hofmann in Nagel's *Handbuch d. Physiol. Menschen*, vol. i., p. 296, Braunschweig, 1909; Roy and Sherrington, *Journ. of Physiol.*, 1890, vol. xi., p. 85 *et seq.*; Bayliss and L. Hill, *Journ. of Physiol.*, 1895, vol. xviii., p. 334 *et seq.*

26 D. Cow, *Journ. of Physiol.*, 1911, vol. xlii., p. 132.

27 Kronecker, verbal communication.

28 Cybulski, quoted by Tigerstedt, *Lehrbuch der Physiologie des Kreislaufs*, p. 359.

29 Ludwig and Cyon, *Ludwig's Arbeiten* for 1866, p. 128; Aubert and Roever, *Pflüger's Archiv*, 1868, vol. i., p. 211.

[30] Roever, Langenbacher and Finkelstein, quoted by Tigerstedt, *op. cit.*, p. 278.
[31] Brunton and Fayrer, *Proc. Roy. Soc.*, 1874, vol. xxii., p. 125; and *Proc. Roy. Soc.*, 1876, xxv., p. 174.
[32] According to Rollett (Hermann's *Handbuch der Physiologie*, vol. iv., p. 153), it was known to Meibomius in 1668, and to Johannes Müller in 1835.
[33] Haller, *Elementa Physiologica*, 1757, tom. i., pp. 410 and 399; and *Memoires sur la Nature Sensible et Irritable des Parties du Corps Animal*, 1756, tom. iv., p. 4.
[34] Senac, *Traité de la Structure du Cœur*, etc., second edition, Paris, 1783, tom. ii., pp. 37 and 38.
[35] Colin, *Compt. rend.*, 1862, tom. lv., p. 495.

CHAPTER II

PHYSIOLOGY OF THE HEART

Movements of the Heart—Heart of the Frog—Origin of the Cardiac Rhythm—Neurogenic and Myogenic Theories—Block Fibres—Differentiation of Protoplasm—Difference between Neurogenic and Myogenic Theories—Origin of Stimuli in the Frog's Heart—Conduction of Stimuli in the Heart—Heart-block—Gaskell's Experiments—Are the Cardiac Nerves useless?—Comparison between the Heart and a Medusa — Experiments of Romanes—Blocking of Stimuli in a Medusa — Interference of Waves — Inhibition—Inhibition in Medusa and in the Turtle's Heart—Inhibition in the Frog's Heart — Action of Vagus—Inhibitory Ganglia—Stannius's Experiments—Refractory Period of the Heart—Experiments of Brunton and Cash—Refractory Period of the Ventricle—Refractory Period of the Auricle—Stimulation of the Venous Sinus — Extra Systoles — Compensatory Pause—Conduction of Stimuli in the Heart, by Nerves as well as by Muscle—Practical bearing of these Experiments.

Movements of the Heart.—In the frog's heart the venous sinus contracts first and drives the blood into the auricles. In the mammalian heart the venous sinus is absent; and therefore in considering the movements of the heart we begin with the auricle, which contracts and drives the blood into the empty ventricle. The ventricle

in turn drives the blood onwards into its corresponding artery, the pulmonary on the right, and the aorta on the left. This rhythmical action continues for some time in a heart after its removal from the body, and if artificial circulation be kept up in the coronary arteries the excised heart may continue to beat for hours or even days.

The movements may be recorded in writing on a revolving cylinder by levers laid on the auricles and ventricle,[1] or connected with them by hooks.[2]

Heart of the Frog.—The heart of the frog being simpler in structure than the mammalian heart, and more easily studied, has been used to a great extent for the purpose of discovering the causation of the cardiac movements. It

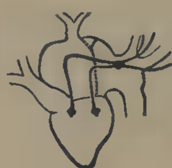


FIG. 4.—Diagram of the frog's heart.

consists of the venous sinus, two auricles, one ventricle, and the aortic bulb (Fig. 4). The vagi nerves pass to the junction of the venous sinus and auricle, and here form a plexus or ganglion, known as Remak's.[3] From this two nerves pass down the auricular septum to the base of the ventricle, where they end in two ganglia, known as Bidder's ganglia.[4] There are also ganglionic cells in the septum

between the auricles, known as Ludwig's ganglion.[5]

Origin of the Cardiac Rhythm.—Two sets of rhythmic movements are necessary to life: (1) the cardiac, (2) the respiratory. The origin of the respiratory rhythm is in a nervous centre in the medulla oblongata, and when this centre is destroyed, or its connection with the muscles of respiration is severed, the respiratory movements cease. As the rhythmic movements of the heart continue after its removal from the body, it is evident that the cause of its rhythm must be situated in the heart itself.

Neurogenic and Myogenic Theories.—Until recently, the rhythmic contraction of the heart was supposed to be due to stimuli originating in nervous ganglia within its walls. This is known as the neurogenic theory. Of late years this has been denied, and the rhythm ascribed to stimuli arising in the cardiac muscle itself. This is known as the myogenic theory.

The difference between these two theories has been so clearly and briefly stated by Tawara, that I cannot do better than translate his words:—

"The myogenic theory assumes that the rhythmic activity of the heart in all animals, both in their embryonic and developed condition, resides in the cells of the cardiac muscle themselves, and that the nervous system possesses merely the secondary function of regulation. It also maintains that the transmission of stimuli between the individual parts of the heart does not occur through nerve fibres, as

the neurogenic theory assumes it does, but through the block fibres."[6]

Block Fibres.—The fibres mentioned under this name by Tawara as conducting stimuli from one part of the heart to another, and regarded by him as muscular, might also be regarded as nervous, for they really consist of protoplasm only partially differentiated, so that it may combine the functions both of muscle and nerve, although it may not contract so perfectly as muscle, nor conduct stimuli so swiftly as nerve. Purkinje's fibres, which form part of the conducting paths in mammalian hearts, are examples of this (Fig. 20).[7] The name of block fibres has been given to the conducting path between auricles and ventricles, because injury to them blocks the transmission of a stimulus from the auricles to the ventricles.[8]

Differentiation of Protoplasm.—In the fresh-water hydra some of the cells appear to have the power of receiving stimuli and also of contracting, in fact, of performing the functions of both nerve and muscle. To these cells the name of neuro-muscular has been given[9] (Fig. 5).

With increasing differentiation the nerve cells acquire greater power of receiving and emitting stimuli, and the nerve fibres of conducting them, but the fibres lose the power of contracting almost entirely, though the nerve cells still retain the power of contracting their dendrons.

Muscle, on the other hand, acquires increased contractile force, but loses to some extent

the power of apparently originating stimuli, so marked in nerve cells. Yet this power is not wholly lost, and even in voluntary muscular

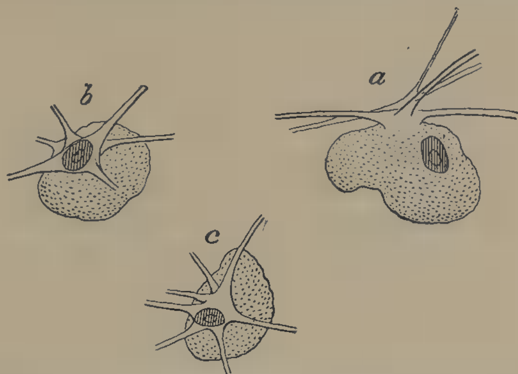


FIG. 5.—Neuro-muscular cells from the fresh-water hydra. *a*, A neuro-muscular cell seen in profile; *b*, a three-quarter view; *c*, a frontal view. (After Ranvier.)

fibre rhythmical contractions may be excited by constant stimuli. Thus, if the Sartorius muscle from a frog's leg, in which the motor nerves have been poisoned by curare, be subjected to a constant stimulus by immersion in distilled water or in a solution of sodium salts,[10] it will contract rhythmically for days. Yet under ordinary circumstances this muscle will only contract when stimulated by its motor nerve. The apex of the frog's heart, which is said to contain no nerve cells,[11] * also ceases to contract when cut off from the rest of the organ; but if it be subjected to a constant

* It contains a fine network of nerve fibres. Compare nerves of arteries, p. 85, and of mammalian heart, p. 54.

stimulus by increased pressure from within, by electricity,[12] or by chemical irritants from without, it will contract rhythmically.[13]

Difference between Neurogenic and Myogenic Theories. — The question between the neurogenic and myogenic theories of cardiac contraction is therefore not so much whether the cardiac muscle *can contract* rhythmically or not without nervous stimuli, but *whether it does so* under ordinary circumstances.

Origin of Stimuli in the Frog's Heart.— In the frog's heart the stimuli which cause rhythmical contraction originate at the junction of the large veins and the venous sinus, and to a less degree at the junction of the auricle and ventricle. According to the neurogenic theory, they are supposed to start in the nerve cells of Remak's and Bidder's ganglia in these places. According to the myogenic, they are supposed to originate in imperfectly differentiated muscle cells at the same points.

Though the ganglion-free apex of the frog's heart will contract rhythmically on the application of a constant stimulus, yet it only responds by a single contraction to a single stimulation. But if the ventricle containing Bidder's ganglia is stimulated in a similar way, it responds by several rhythmical contractions;[14] and when it is subjected to such chemical irritants as have no action on the apex, or to warmth which is also without action on the apex, it responds by a series of contractions.[15] These as well as other facts show that although the muscle of the frog's heart does possess the power of

rhythmical contraction apart from any ganglia, yet it is from the ganglia that the stimuli to rhythmical contraction usually proceed.

In regard to those parts of the heart from which the stimuli to contraction proceed, it might be better to speak of *conversion* rather than of *origination* of stimuli, because they probably do not generate a new stimulus, but only convert a constant stimulus into a rhythmical one, just as the ganglion-free apex responds to a constant mechanical or chemical stimulus by rhythmic contractions. The difference between the apex which is without, and the sinus which contains ganglia, is not so much one of kind as of degree. When Stannius's ligatures are applied under oil, so that the heart is not exposed to the stimulus of the air, the ventricle only contracts when Bidder's ganglia are stimulated by the application or removal of the ligature.[16]

Conduction of Stimuli in the Heart.—According to the neurogenic theory, the stimuli are transmitted from the venous sinus to the auricle, and from the auricle to the ventricle, by nerve fibres; but the quotation I have already given from Tawara (p. 27) shows that those who hold the myogenic theory entirely deny this transmission by nerve fibres, and assert that it occurs only through the block fibres already mentioned, and through the muscular fibres of the heart itself.[17]

Heart-block. Gaskell's Experiments.— It was discovered by Gaskell that when the frog's heart is placed in a clamp, the jaws of which lie

in the groove between the auricles and ventricle, no alteration occurs in the beats so long as the clamp exerts no pressure on the heart. But as the jaws of the clamp are gradually tightened the cardiac rhythm becomes altered so that instead of the ventricle beating at the same rate as the auricle, it may only beat once (Fig. 6) for every two beats of the auricle, then for every three, then for every four, and so on.[18] The compression seems to block the passage of

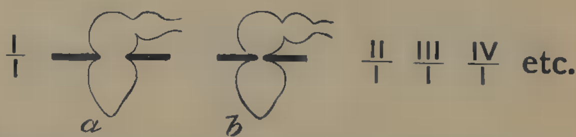


FIG. 6.—Diagram to illustrate Gaskell's experiment of cardiac block. At *a* the jaws of the clamp hold the heart without compressing it, and each beat of the auricle is succeeded by one of the ventricle, as shown by the figure $\frac{\text{I}}{\text{I}}$. At *b* the heart is compressed, and its rhythm disturbed, so that one beat of the ventricle only occurs for several of the auricles. This is indicated by the Roman numbers, the upper line of which shows the number of auricular, and the lower of ventricular beats.

stimuli from the auricles to the ventricle, until they have accumulated sufficient strength to force their way in spite of the obstacle. To this condition the name of heart-block is applied. The same result is obtained by partially dividing the fibres connecting the auricle and ventricle.

Are the Cardiac Nerves useless? — The myogenic theory easily explains the rhythm of the heart and heart-block so far, but there are other phenomena which are not easily explicable, except on the hypothesis that both nerves and muscle participate in the cardiac rhythm.

The nerves in the heart are extraordinarily abundant, and in order to explain what I believe to be their object I may perhaps be allowed to employ a simple comparison. A railway train, when once started, usually proceeds from station to station without interference; but alongside the rail, or overhead, run the telegraph wires, and at any station the progress of the train may be stopped by a message sent by the telegraph. You will notice also that in many railways an electric bell rings before the train actually appears, so that all preparations may be made for its arrival. In the heart the transmission of stimuli by the cardiac muscle would correspond to the passage of the train; the transmission by the nerves would correspond to the telegraph, by which the movement of the ventricle might either be stopped, even after an impulse had been sent on from the auricle (Fig. 22, p. 69), or, on the other hand, the ventricle might be prepared to respond more quickly to the stimulus passing from the auricle. The advantage of such a preparation is evident from Romanes's experiments on medusæ, in which stimuli did not always produce the proper effect unless they had been preceded by another stimulus which prepared the protoplasm to react.

Comparison between the Heart and a Medusa. Experiments of Romanes. — The nervous and muscular structures of the heart are very intimately related, so that it is extremely difficult to determine the part played by each, and it is easier to observe the relationship between protoplasm and nerves in the

medusæ, or jelly-fish, where they can be more easily separated, and thus gain some light upon the function of each on the heart. A number of observations were made upon medusæ by Romanes. A medusa consists of a bell-shaped piece of contractile protoplasm, from the centre of which a polyp descends, and round the margin of the bell is a nervous gangliated chain and a fringe of mobile tentacles (Fig. 7). For the

Fig. 7.—Diagram of a medusa (Tiaropsis), about one-third natural size, with a strip of contractile tissue cut from the bell, but left attached at one end.

purpose of description, we may put the polyp, for the present, out of account, and if we invert the bell we find that it bears a very close resemblance to the ventricle of the frog, which, like it, consists of a contractile portion with ganglia at its margin. When the complete medusa is placed in sea-water, the bell contracts rhythmically, just like a heart.[19] When the nerves are removed by cutting off the marginal strip which contains them, the bell ceases to contract; but it will recommence if a constant

stimulus, either chemical or electrical, be applied to it.[20] In this respect it completely resembles the apex of the frog's heart. Moreover, when a stimulus is first applied it may not appear to act, but when applied several times the contractions it induces are stronger and stronger up to a certain maximum, so as to produce the appearance of a staircase—a phenomenon which was also observed by Bowditch in the case of the heart.[21] When a strip of medusa containing the ganglia is detached only at one end from the animal and is left attached at the other, irritation of the strip will cause a wave to pass along, which is of two kinds.[22] The first is that of contraction in the protoplasm, and the other is a nervous stimulus, which makes itself evident by the movements of the tentacles. These waves generally pass together, the nervous wave being usually a little in front of the contraction-wave; but it may also occur, as is shown by the movements of the tentacles, without any contraction-wave in the protoplasm of the strip. This nervous wave is more easily excited than the contraction-wave, so that it may be started by stimuli which are too slight to affect the contractile substance, the ganglia apparently being more sensitive than the protoplasm. For this reason also when the nervous wave reaches the bell it will cause it to contract if the ganglia are still present in the bell; but if these have been removed, the nervous wave has not the power to stimulate the protoplasm of the bell, which, consequently, remains motionless.[23]

Blocking of Stimuli.—The passage of stimuli along the strip of medusa may be hindered or prevented, as in the heart, by compressing it, by partially dividing it so as to narrow it, or by straining it so as to injure it; or by poisons, such as chloroform, ether, alcohol, strychnine, and curare. As one would expect from different kinds of injury, sometimes the contraction-wave is blocked first and sometimes the nervous wave. When the block is only partial, it may happen that several of these waves come up to it before one can pass across, just as in heart-block.[24]

Interference of Waves.—In order to explain

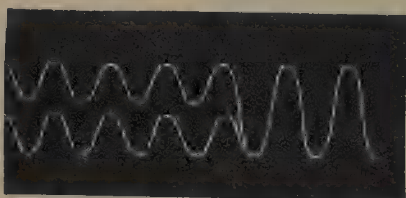


FIG. 8.—Diagram of two sets of waves reinforcing each other, so as to produce a double effect.

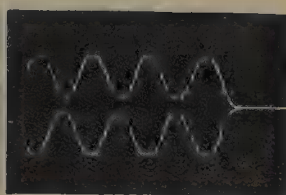


FIG. 9.—Diagram of two sets of waves interfering with each other.

some of the phenomena of inhibition in medusa and in the heart, it may be well to refer to the interference of waves in general. When two sets of waves travelling from the same point, and at the same rate, combine so that the crests and hollows of the waves in each set coincide, the height of the waves becomes double what it was before (Fig. 8). But if one set of waves should be thrown half a wave-length behind the other, the crests of one set will fill up the hollows

of the other, and there will be no wave at all (Fig. 9). This phenomenon is said actually to occur in the harbour of Batscha, where there are two channels, one of which is slightly longer than the other. It is just enough to throw the set of waves travelling through it half a wave-length behind those travelling through the other, so that when they meet the water becomes perfectly still.[25] The same occurs with sound, so that two tones may destroy each other. In the winter of 1861-2 I witnessed Professor P. G. Tait show the marvellous experiment of two lights making darkness. So far as I recollect this was done by throwing two equal beams of sunlight upon a wall. One of these, however, was passed through a plate of tourmaline, which threw the waves of light in this beam nearly half a wave-length behind those in the other. By means of a prism this beam could be thrown upon the other. When this was done the spot of light on the wall, instead of becoming brighter, was eclipsed, and when the experiment was finished, instead of two bright spots of light on the wall there was only one, much dimmer than either had been before. Had the one beam been exactly half a wave-length behind the other, instead of only nearly so, there would have been no light at all.

If the retardation of one beam is still greater, so that it falls a whole wave-length behind the other, the crest of the waves will again coincide, and they will again reinforce instead of interfering with each other. If the waves are of different lengths, they will sometimes

strengthen and sometimes weaken each other (Fig. 10).*

Inhibition.—By this term is usually meant the prevention of a movement which would otherwise occur.[26] Inhibition may be produced in different ways. Thus the hand may be kept motionless although the biceps is contracting strongly, and would bend the elbow at once, if the triceps did not contract at the same time sufficiently to counteract the biceps. But the hand may also remain motionless and both these

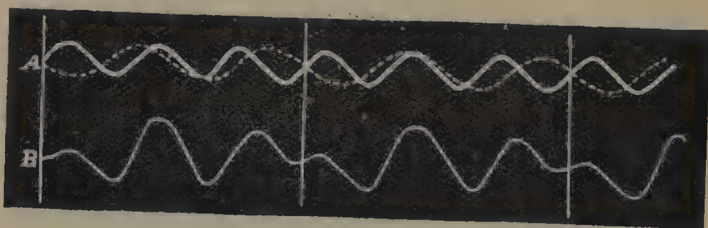


Fig. 10.—Diagram showing the effect of interference of two systems of different wave-lengths, the dotted line in A with 4 waves to 7 of the complete line. The resultant is shown in B. (From Ganot's *Physics*.)

muscles remain inactive even when the hand is pricked or injured, and would naturally be moved if the will of its owner did not prevent it. In this case the inhibition occurs in the central nervous system, and the exact way in which it does so is not at present known, although it is probably due to interference of some sort between nervous impulses.

* Alex. Forbes has produced rhythmical contraction of voluntary muscle reflexly by concurrent stimulation of excitatory and inhibitory nerves.—*Roy. Soc. Proc.*, 1912, vol. lxxxv., p. 292.

Inhibition in Medusæ and in the Turtle's Heart.—It has been found by A. G. Mayer * that a strip of the sub-umbrella of a scyphomedusa, cut in the shape of a ring, will continue to pulsate rhythmically if a contraction-wave be once started in it. This may be done by the application of various chemical or electrical stimuli. The contraction arises at the point of stimulation, wherever this may be. It may spread from this point as two waves travelling in different directions round the ring. If they are equally strong they block each other when they meet, and all movement ceases until a new stimulus is applied and a new contraction started.† But if one is stronger than the other it goes on, while the weaker wave is obliterated.[27]

The ventricle of the Loggerhead Turtle's heart when cut into rings behaves in a similar manner.[28]

Inhibition in the Frog's Heart. Action of the Vagus. — In 1845 the brothers Ernest Heinrich and Eduard Weber discovered that, in the frog, electrical irritation of the medulla oblongata, or of the vagus nerves which pass from it to the heart, causes both the auricles and ventricle to cease beating and to stand still in diastole.[29] This stoppage they attributed to action of the vagi nerves upon those nervous structures in the heart which were regarded as

* A. G. Mayer, advance print from the *Proceedings of the Seventh International Zoological Congress*, Boston, 19th to 24th August 1907.

† M. Schiff found that peristaltic waves may be produced in voluntary muscle, and that these may cross each other without interference. Moleschatt's *Untersuchungen*, 1837, vol. i., p. 84.

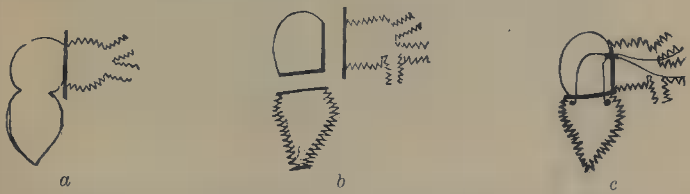
originating its rhythmical movements, in somewhat the same way as the brain affects the motor cells in the cord, and keeps the hand still if its owner wishes to do so, in spite of irritation to the hand. The structures through which the vagi acted they regarded as inhibitory ganglia in the heart itself. This view seems to receive confirmation from the fact that when Remak's ganglia are stimulated the auricles and ventricles stand still while this sinus continues to pulsate.

Inhibitory Ganglia. Stannius's Experiments.—In 1852 Stannius[30] showed that if a ligature is tied around the heart exactly at the spot where the venous sinus joins the auricles, or if the heart is cut across at this point, the auricles and ventricles stand still, while the sinus and vena cava continue to beat as before (Fig 11, *a*). This result is easily explained on the myogenic theory by the supposition that the muscular tissue in the sinus and auricles is the source of the stimuli to rhythmic action, and the auricles and ventricle stand still because the ligature prevents these stimuli from reaching them, just as the clamp cut off the ventricle in Gaskell's block experiment.

Another experiment is not so easy to explain on this theory. If a second ligature be tied around such a heart exactly at the groove between the auricles and ventricle (Fig. 11, *c*), or if a cut be made here, the auricle remains still as before, but the ventricle commences to beat again, though at a slower rate than the sinus (Fig. 11, *b*).

This seems to necessitate the assumption

that there is a second motor centre, either nervous or muscular, in the ventricle itself, whilst the auricles do not possess such a centre, and therefore stand still.



FIGS. 11 and 12.—AUTHOR'S DIAGRAMS TO ILLUSTRATE THE EXPERIMENTS OF STANNIUS.

FIG. 11.—*a*, Diagram of frog's heart ligatured at the junction of the venous sinus with the auricles. The venæ cavæ and sinus are represented with a crenated outline resembling the tracing which their beats might give if recorded on a revolving cylinder. The auricle and ventricle being motionless would only trace a straight line if connected with a recording apparatus. Their outline is therefore represented by a straight line. *b*, Diagram of a frog's heart in which sections have been made at the junction of the sinus with the auricles, and at the auriculo-ventricular groove. The sinus and ventricles pulsate, whilst the auricles remain motionless. The beats of the ventricle are represented as slower than those of the auricle. *c*, The same as *b*, but with the parts of the heart separated by ligature instead of section.

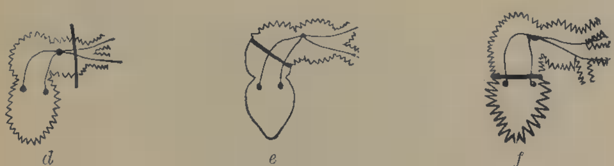


FIG. 12.—*d*, Diagram of heart with ligature round the venous sinus. *e*, Diagram of heart with ligature round middle of auricles. *f*, Diagram of heart with ligature in the auriculo-ventricular groove. The pulsations of the ventricle are much slower than those of the auricle and venous sinus. This in indicated by the larger dentation of the outline of the ventricle.

But a third experiment seems to show that this explanation is insufficient. If instead of tying a ligature at the junction of the venous sinus and auricles it be tied round the auricles

low down, near their junction with the ventricle, the sinus and upper part of the auricles continue to beat, but the lower part of the auricle and the ventricle after one or two pulsations (Fig. 12, *e*) stand still. This appears to show that in the lower part of the auricles there is some inhibitory apparatus which prevents the ventricle from beating, as it would do if the whole of the auricle were separated from it either by ligature or section. The portion of auricle which prevents the ventricle from beating may be very small. I have seen the ventricle of a frog's heart, from which the venous sinus and auricles appeared at first sight to have been completely cut away, obstinately refuse to beat, until a fragment of auricle about the size of a pin's head, which had at first been overlooked, was cut away. Then the ventricle at once began to pulsate rhythmically. The phenomenon was like a big horse held still by a small jockey, whose removal at once allowed the horse to go on. It is very difficult to explain this on the ordinary myogenic theory, but easy if we suppose some of the ganglion cells in the auricle to have an inhibitory action.

An inhibitory apparatus of some kind appears to be present in the venous sinus also, for stimulation of this part of the heart will produce still stand of the whole heart.[31]

Refractory Period of the Heart.—Throughout nature, whenever an action, which would otherwise be continuous, meets with a resistance it tends to become intermittent. Thus the wind usually blows in gusts, each of which is followed

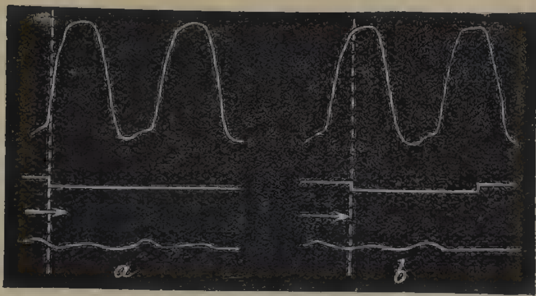


FIG. 13.

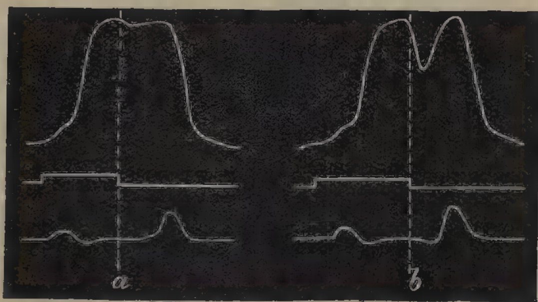


FIG. 14.

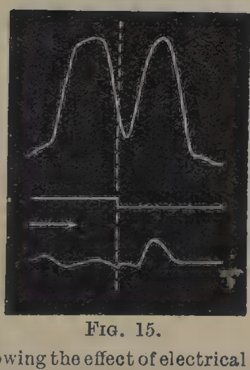


FIG. 15.

FIGS. 13, 14, and 15.—Showing the effect of electrical stimulation of the frog's heart. The upper tracing shows the beats of the ventricle, the lower those of the auricle, and the depression in the middle line shows the time of applying the stimulus by breaking the current. The dotted line shows the relation of this to the contraction. Fig. 13 shows stimulation during the refractory period; Figs. 14 and 15, after this period has passed.

by a lull, and the flow from a fountain usually occurs in jets. It seems as if time were required for the accumulation of energy to overcome the obstacle, and when this is done the energy spends itself, and then another period of rest must ensue to allow of a fresh accumulation. As already mentioned (p. 5), action is necessarily followed by sleep. In the frog's heart there is a time during which the ventricle does not contract in response to stimulation, either from the sinus or auricle, or directly applied to the ventricle itself. This was discovered by Kronecker,[32] and later by Marey,[33] who gave it the name of "Refractory Period." Its time relations and the electrical changes which accompany it were investigated by Sir John Burdon-Sanderson and Mr Page.[34]

Experiments of Brunton and Cash.—It was also experimented on by Dr Cash and myself, and the results we obtained are shown in the accompanying figures.[35]

Refractory Period of the Ventricle.—From these it will be seen that during the greater part of its systole electrical stimulation of the ventricle itself has no effect, but the ventricle responds to the stimulus when it is applied just as the systole is ending and during the diastole.

Refractory Period of the Auricle.—This is not so well marked as that of the ventricle, but the tracing in Fig. 16 shows that stimulation of it during its diastole may cause it to contract. This induced contraction, instead of being followed by a contraction of the ventricle, is succeeded by a prolonged pause, and when the

stimulus is applied at the height of its contraction only a prolonged pause is produced both in auricles and ventricle.

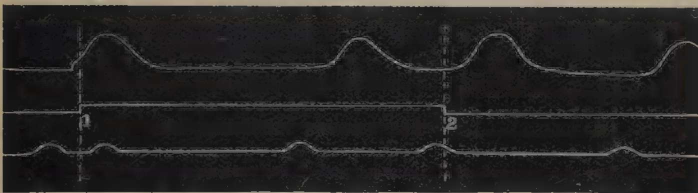


Fig. 16.—Shows effect of stimulation of the auricle on the beats of the auricle itself and of the ventricle.

Stimulation of the Venous Sinus.—Stimulation of the venous sinus causes reduplication of the auricular beat, but absence of the ventricular beat which ought to have followed it; just as two trains may be started in almost immediate succession from one station, but the second may be stopped by a telegraphic message (Fig. 17).

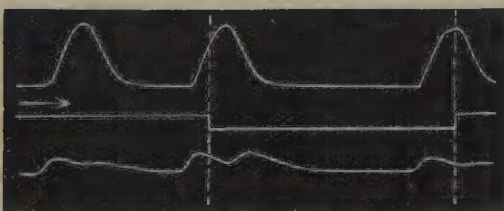


Fig. 17.—Shows the effect of stimulation of the venous sinus.

It may be considered that this effect is due to extension of the stimulus to the auricle; but I do not think this is the case in the experiments made by Cash and myself, because the tracing, Fig. 17, was obtained with a minimal stimulus

which would not extend to the auricle. It may be said that the reason the ventricular beat did not follow the induced auricular beat was because the stimulus proceeding from the auricle reached the ventricle during its refractory stage. But a comparison of Fig. 17 with Figs. 14 and 15 will show that the stimulus from the second auricular beat must have reached the ventricle after its refractory period had passed.

Engelmann found that stimulation of the sinus may cause systole of the ventricle with absence of the auricular beat.[36]

Extra Systoles.—Except during the refractory period, a stimulus applied to the ventricle itself, to the auricle, or to the venous sinus will produce a ventricular contraction. To such a contraction occurring out of the usual rhythm the name of extra systole is given.[37] Extra systoles have been classified into ventricular, auricular, and venous, according to the part from which the stimulus proceeds.[38]

Compensatory Pause.—An extra systole is generally followed by a longer pause than normal, so that its occurrence does not necessarily quicken the pulse, and two systoles close together followed by a long diastole generally occupy the same time as two normal beats. If the extra systole is induced by a stimulus at the vena cava it is not followed by a compensatory pause.[39]

Conduction of Stimuli in the Heart by Nerves as well as by Muscle.—Engelmann's experiment, in which he showed that a heart cut into zigzag strips so as to divide any nerves

in it, would transmit a contraction caused by a stimulus to one end of the strip,[40] shows that the cardiac muscle can conduct a stimulus. But the experiments of Cash and myself, which were not only very numerous, but very varied, show, we think, that in the heart, just as in a medusa, there are two channels, one muscular and the other nervous, by which stimuli are conducted from one part of the heart to another. They seem also to show that nervous conduction may interfere with muscular conduction (Fig. 17).

Practical Bearing of these Experiments.—There is now a tendency to explain intermittent pulse by the supposition that it is caused by some kind of block in the transmitting structures, whilst these experiments show that the intermissions may occur without any block except that caused by interference of stimuli (*vide* p. 36).

The practical importance of the myogenic and neurogenic theories is that if the myogenic theory be true to the exclusion of the neurogenic, only those drugs will be of use in cardiac disease which act on the cardiac muscle, and such drugs as strychnine, which has a powerful action on nerves but little or none on muscle, will be of little or no use.

LITERATURE.

1 Lauder Brunton, *Journ. Anat. and Physiol.*, April 1876, vol. x., p. 602; Ranvier, *Leçons d'Anatomie Générale, année* 1877-78 (Paris, 1880: J. B. Baillière et Fils), p. 42.

2 Gaskell, *Phil. Trans.*, 1882, p. 994.

3 Remak, "Neurologische Erlauterungen," *Müller's Arch. f. Anat. u. Physiol.*, 1844, p. 463.

[4] Bidder and Rosenberger, *Müller's Arch. f. Anat. u. Physiol.*, 1852, p. 172 *et seq.*

[5] Ludwig, *Arch. f. Anat. u. Physiol.*, 1848, pp. 139-143.

[6] S. Tawara, *Das Reizleitungssystem des Saügethierherzens* (Fischer, Jena, 1906), p. 185.

[7] Purkinje, "Mikroscopisch - neurologische Beobachtungen," *Müller's Archiv*, 1845, p. 281; Ranvier, *Leçons d'Anatomie Générale sur le Système Musculaire* (Paris: A. Delahaye & Co., 1880), p. 325 *et seq.*

[8] Tawara, *op. cit.*, p. 185.

[9] Ranvier, *Leçons d'Anatomie Générale sur le Système Musculaire*, 1880, p. 300.

[10] Hermann, *Handb. der Physiol.*, 1879, Bd. i., Theil 1, p. 113; Biedermann, *Sitzungsb. d. k. Akad. d. Wiss. math.-phys. Cl.*, 1880, Bd. lxxxii., 3 Abt., p. 257 *et seq.*; Biedermann, *Electro-physiology*, trans. F. A. Welby, 1896 (London: Macmillan & Co.), vol. i., p. 105.

[11] Ranvier, *Leçons*, 1877-8, pp. 47 and 143.

[12] Bowditch, *Ber. d. sächs. Gesellsch.*, 1871, p. 682, and *Ludwig's Arbeiten*, 1871, p. 176; Merunowicz, *Ludwig's Arbeiten*, 10$^{\text{ter}}$ Jahrg., for 1875, p. 140, and *Ber. d. sächs. Gesellsch.*, 1875, p. 254; Eckhard, *Beiträge z. Anat. u. Physiol.*, 1888, p. 153; Ranvier, *Leçons*, 1877-8, pp. 47 and 143.

[13] Langendorff, *Arch. f. Anat. u. Physiol., Phys. Abt.*, 1884, Supp. Bd., p. 8 *et seq.*

[14] Munk, 1861, *Beilage z. Tagebl. d. Naturforscher Versaml. zu Speyer*, p. 46, quoted by Tigerstedt, *Lehrb. d. Physiol. d. Kreislaufes*, p. 198.

[15] Marchand, *Pflüger's Archiv*, 1878, vol. xviii., p. 513.

[16] Goltz, *Archiv f. path. Anatomie*, 1861, vol. xxi., p. 201 *et seq.*

[17] For a full discussion of this question, *vide* Gaskell on "The Contraction of the Cardiac Muscle," Schäfer's *Physiology*, vol. ii., pp. 169-227 (Edin. and London: Pentland, 1900).

[18] Gaskell, *Phil. Trans.*, London, 1882, vol. clxxiii., pp. 999 and 1031.

[19] Romanes, *Phil. Trans.*, vol. clxvi. (1876), p. 270.

[20] Romanes, *Phil. Trans.*, vol. clxxi. (1880), p. 163.

[21] Romanes, *Phil. Trans.*, vol. clxvii. (1877), p. 688; Bowditch, *Ludwig's Arbeiten*, 1871, p. 155.

[22] Romanes, *Phil. Trans.*, vol. clxxi. (1880), p. 191.
[23] Romanes, *Phil. Trans.*, vol. clxvi. (1876), p. 272.
[24] Romanes, *Phil. Trans.*, vol. clxvi. (1876), pp. 293 and 294. See also Romanes, "Jelly Fishes, Star-fish, and Sea-urchins," vol. iv. of *International Scientific Series* (Kegan Paul, Trench & Co., London, 1885).
[25] Sir John F. W. Herschel, *Phil. Magazine*, vol. iii., 1833, p. 405.
[26] For a discussion of this subject, *vide* Lauder Brunton on "Inhibition Peripheral and Central," *West Riding Asylum Reports*, vol. iv., 1872; and "On the Nature of Inhibition, and the Action of Drugs upon it," *Nature*, 1st March 1883, vol. xxvii., p. 419.
[27] Romanes, *Phil. Trans.*, vol. clxvii. (1877), pp. 718 and 729; Alfred Goldsborough Mayer, "The Cause of Rhythmical Pulsation in Scyphomedusæ," advance print from the *Proceedings of the Seventh International Zoological Congress* (Boston, 1907; Cambridge, Massachusetts, 1909), p. 1.
[28] A. G. Mayer, *op. cit.*
[29] Eduard Weber, *Wagner's Handwörterb. d. Physiol.*, 1846.
[30] Stannius, *Müller's Arch. f. Anat. u. Physiol.*, 1852, pp. 85-92.
[31] A. B. Meyer, *Hemmungsnervensystem des Herzens*, Berlin, 1869; Schmiedeberg, *Ludwig's Arbeiten*, 1870, p. 44.
[32] Kronecker, *Beiträge z. Anat. u. Physiol.* (C. Ludwig, gewidmet, 1874), p. 181.
[33] Marey, *Travaux du Laboratoire*, 2, p 78: 1876.
[34] Burdon-Sanderson and Page, *Journ. of Physiol.*, 1880, vol. ii., p. 384; 1884, vol. iv., p. 327.
[35] Brunton and Cash, *Roy. Soc. Proceed.*, 1881, vol. xxxii., p. 383; 1883. vol. xxxv., p. 455.
[36] Engelmann, *Pflüger's Archiv*, 1894, vol. lvi., p. 149.
[37] Engelmann, *op. cit.*
[38] Hirschfelder, *Diseases of the Heart and Aorta*, (London and Philadelphia: Lippincott, 1910), p. 69.
[39] Martin Flack, *Further Advances in Physiology*, p. 52 (London: Edward Arnold, 1909).
[40] Engelmann, *op. cit.*, 1875, vol. xi., p. 466 *et seq.*

CHAPTER III

PHYSIOLOGY OF THE MAMMALIAN HEART

Muscular Structure of the Mammalian Heart—Nature of the Cardiac Muscle—Intrinsic Nerves of the Heart—Contraction of the Mammalian Heart—Active Dilatation of the Heart—Characteristics of the Heart—Origin of Stimuli in the Mammalian Heart—Nodes—Position of the Nodes—Structure of the Nodes—Connections of the Nodes—Bundle of Stanley Kent and His—Pacemaker of the Heart—Nodal Rhythm—Heart-block—Cause of Heart-block in Man—Functional Heart-block—Nœud Vital of the Heart—Kronecker and Schmey's Experiments—Fibrillation—Extrinsic Nerves of the Heart—Functions of these Nerves—Complex Functions of the Vagus—Afferent and Sensory Nerves of the Heart—Pain—Depressor Nerve—Mode of Action of the Vagus on the Heart—Opposite Effects of the Vagus on Heart-block—Trophic Action of the Vagus—Accelerator Nerves of the Heart—Reflex Stimulation of the Cardiac Nerves—Reflex Stimulation of Inhibition—Valves of the Heart—Sounds of the Heart—Double Nature of the Heart—Right Ventricle.

Muscular Structure of the Mammalian Heart.—By using Purkinje's method[1] of boiling a calf's heart for half an hour in vinegar, it is easy to ascertain that the ventricles are composed of muscular fibres which run more or less

longitudinally on the inside and outside, and transversely in the middle of the ventricular

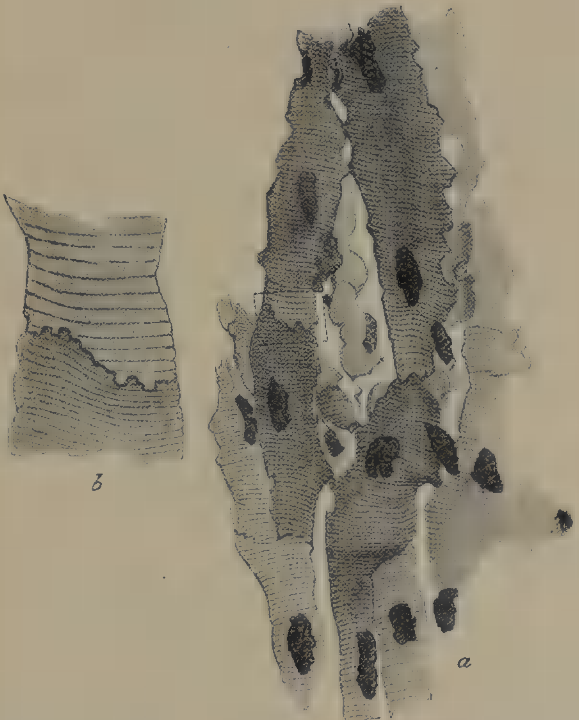


FIG. 18.—Cells taken from a heart in fibrillation. The preparation shows that the intercellular limits separate very sharply parts with striæ widely apart from others with striæ close together, whilst in the interior of the cells numerous transitions may be observed. The larger figure (*a*) is magnified 750 diameters by an apochromatic objective, No. 2 of Zeiss, and compensating eyepiece, No. 6. The small portion (*b*) strongly magnified was observed with Zeiss's No. 2 objective and a compensating eyepiece, No. 18, with an intense illumination. Its position in *a* is marked by the rectangle of dotted lines. (After Kronecker and Imchanetzky.)

wall. These are connected by oblique fibres, and some of them end in the musculi papillares.

The course of these fibres has been ascertained much more exactly by C. Ludwig and others.*

Nature of the Cardiac Muscle.—The cardiac muscle is unlike any other muscle in the body, either voluntary or involuntary. Its fibres are not composed of spindle-shaped cells, but of more or less quadrangular cells which are sometimes joined, end to end. They have a tendency to divide at the end, and the divisions anastomose with those from other fibres, thus producing a kind of network (Fig. 18). It was formerly supposed that they were connected with one another by some cement substance, because under the microscope divisions between them appeared quite definite. Of late years there has been a tendency to suppose that they really form a syncytium or united cell, through all parts of which stimuli can be propagated in any direction.[2] This view, however, cannot be accepted without limitation, because in fibrillation a single cell may be found contracted while the adjacent cells are relaxed[3] (Fig. 18).

Intrinsic Nerves of the Heart.—The nerves of the heart may be regarded as consisting of two kinds. *First*, neuro-muscular, forming nodes and fibres;[4] *second*, ordinary ganglia and nerve fibres. These are very numerous,[5] and though opinions may be divided in regard to the part they take in originating the cardiac contractions or conveying stimuli from one part of the heart to another, physiologists are

* C. Ludwig, *Lehrbuch der Physiologie des Menschen*, vol. ii., p. 78 *et seq.* (Leipzig and Heidelberg: Winter, 1858); also Quain's and other textbooks of anatomy.

generally agreed that they serve to co-ordinate the action of the heart with that of the vessels.

So numerous are the nerves of the heart, that Dr Robert Lee says,[6] "It can be clearly demonstrated that every artery distributed throughout the walls of the uterus and heart, and every muscular fasciculus of these organs, is supplied with nerves upon which ganglia are formed." This statement made by Lee in 1849, has been to a great extent confirmed by Retzius,[7] who limits it, however, by saying that it is hardly possible that every muscular fibre receives a nerve, and that in fact many fibres may be seen which are not in contact with nerve endings. Retzius, Ramon y Cajal,[8] and H. J. Berkeley[9] all agree that the nerve terminations form a network round the muscular fibres, and that upon them varicosities may be observed. These are regarded by Berkeley as bipolar nerve cells. Heymans and Demoor[10] have again investigated the whole question, and while they find bodies which greatly resemble ganglionic cells lying between the muscular fibres, they are inclined to consider them as connective protoplasmic cells. They agree, however, with the others in regard to the existence of a fine network of nerve fibrils surrounding the muscular fibres. This network, as figured by them in Fig. 34, Plate xviii., and others of their work, is almost exactly like that upon arteries (Fig. 25, p. 85).

Intrinsic Sensory Nerves.—It would appear from some experiments of von Basch and A. Fröhlich[11] that some of the nerves in the heart are sensory, and give rise when stimulated to

extra systoles; for when a limited part of the epicardium is carefully painted with a solution of cocaine, an electrical stimulus applied to that part requires to be greatly increased in order to produce an extra systole, while the

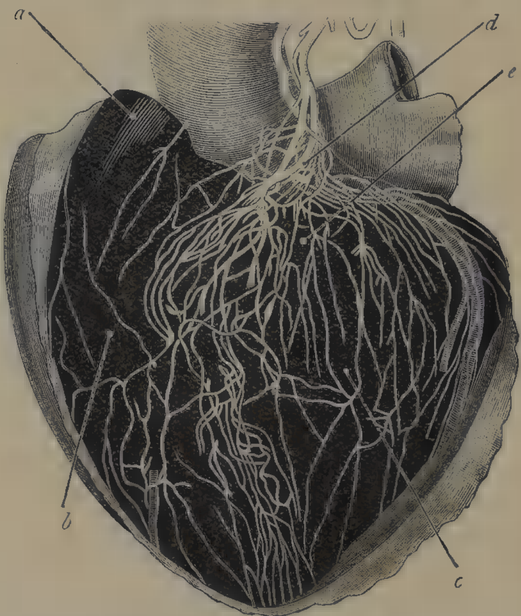


FIG. 19.—Anterior cardiac plexus of nerves. (After Robert Lee.) *a*, Origin of pulmonary artery which has been completely removed; *b*, anterior surface of the right ventricle; *c*, anterior surface of the left ventricle; *d*, left vagus; *e*, the trunk of the left coronary artery ossified and completely surrounded with ganglia and nerves, which are distributed over the whole surface of the ventricle to the apex.

other parts of the heart retain their normal sensitiveness; and other experiments show that this diminution in sensibility is not due to any alteration in the muscle underlying the epicardium.

Contraction of the Mammalian Heart.—In mammals, as I have already mentioned (p. 21), the vena cava and pulmonary veins may continue to beat rhythmically after the rest of the heart has ceased to beat, but usually the contraction of the heart begins in the auricles at their junction with the veins, and passes on to the ventricles. Electrocardiograms seem to show that the ventricle begins first to contract slightly at the base, next the apex contracts, and then the base again forcibly.[12] This arrangement is well adapted to drive the blood completely out of the heart, for the slight contraction at the base will contract the auriculo-ventricular rings and prevent regurgitation, the simultaneous contraction of the musculi papillares and of the apex will have the double effect of keeping the valves tight and driving the blood on into the vessels, while the final contraction at the base will finish the expulsion of the ventricular contents.

Active Dilatation of the Heart.—This is greatly disputed, but there seems some evidence to show that under the influence of vagus stimulation a slight actual dilatation occurs.[13]

Characteristics of the Heart.—The ventricular beat is a single muscular contraction, and not a tetanus.[14] Very strong electric currents applied to any part of the heart will paralyse the cardiac nerves and cause fibrillation (p. 63) of the muscle, but do not cause tetanus. Frequent electrical stimuli of moderate strength, such as would cause tetanus in a voluntary

muscle, accelerate the beats of the heart. Stimulation of the heart causes it to beat either with its full strength or not at all. This observation was made by Bowditch, and formulated by Ranvier in the expression, "All or none," an expression which has since been called "Bowditch's law."[15] The activity of the ventricle has been described by Gaskell as depending on five factors:—1*st*, Rhythm of the stimuli (chronotrope); 2*nd*, rapidity of their conduction in the heart (dromotrope); 3*rd*, excitability to stimuli (bathmotrope); 4*th*, contraction force (inotrope); 5*th*, tonicity.[16] To these functions the names which are enclosed in brackets were given by Engelmann,[17] and the increase or diminution in them are indicated by the terms positive and negative. Thus, if irritation of the vagus slowed the heart by lessening the production of stimuli in the heart, it would be said to exercise a negative chronotrope effect; if it slowed their conduction from auricle to ventricle, it would exercise a negative dromotrope effect; and if it lessened the strength of the ventricular contraction, a negative inotrope action.

Origin of Stimuli in the Mammalian Heart. Nodes.—The stimuli to contraction are supposed to arise from two nodes, which consist of imperfectly differentiated muscle or neuromuscular tissue.[18] It is to be remembered, however, that at these places where these nodes occur numerous ganglion cells are also present and are often arranged in groups corresponding to Remak's, Ludwig's, and Bidder's ganglia in the frog's heart.[19]

The first of these is known as Keith and Flack's, or sino-auricular, or S-A node. It is situated in the right auricle, between the mouths of the venæ cavæ.[20] This part of the auricle is sometimes called the auricular canal, and corresponds to the venous sinus in the frog. A second and similar node, called the auriculo-ventricular or A-V node, is situated in the posterior part of the right auricle, near the septum below, and to the right of, the coronary sinus.[21]

Structure of the Nodes.—They both consist of a complicated network of peculiar muscular fibre, in which transverse striation is very indistinct. They have few fibrillæ and much protoplasm.[22]

Connections of the Nodes.—These two nodes are connected by muscular fibre in the auricular septum.[23]

Bundle of Stanley Kent and His.—From the A-V node a bundle of partially differentiated fibres is given off, which has been described by Stanley Kent[24] and His, junior,[25] and carefully examined by Tawara.[26] It is generally known shortly as the bundle of His. It passes forwards on the intra-ventricular septum, and then divides into two branches which run forwards towards the apex of each side of the septum, and break into fibres which end in the musculi papillares, and appear to be identical with the fibres first described by Purkinje, and known by his name. These fibres are only striated on their periphery, and may be regarded as neuro-muscular, possessing the properties both of muscle and nerve (Fig. 20).

Pacemaker of the Heart.—The S-A node is supposed to be more sensitive than the A-V node, and usually to act as the pacemaker of the heart.[27]

Nodal Rhythm.—When the S-A node fails to act the A-V node is capable of initiating a rhythm of its own, just as the upper part of the frog's ventricle does when entirely separated

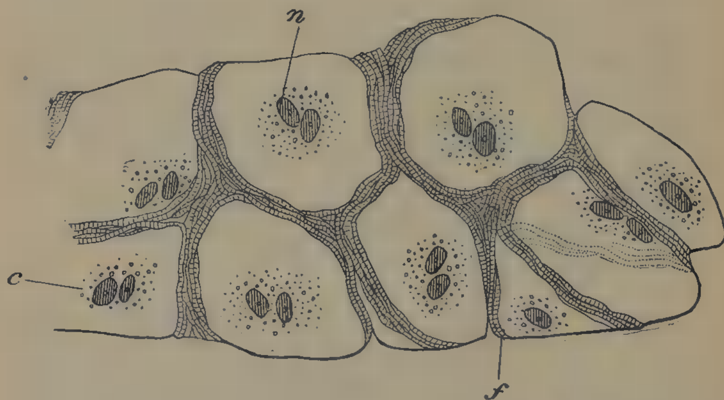


FIG. 20.—Purkinje's fibres from a sheep's heart. *n*, Nuclei; *c*, protoplasm; *f*, striated muscular substance. (After Ranvier, *Leçons d'Anatomie Générale sur le Système Musculaire* (Paris: Delahaye & Co., 1880), p. 300.)

from the auricle (p. 30). This has been called by Mackenzie, Nodal Rhythm.[28]

Ventricular contractions due to stimuli arising from the usual place, viz. the S-A node, have been termed nomotopic, and those arising from other places ectopic.[29]

Heart-block.—The same phenomena that Gaskell observed (p. 32) when the auriculo-ventricular groove in the frog's heart was compressed by a clamp have been found to occur

also in the mammalian heart when the conduction between the auricle and ventricle has been lessened or destroyed by a ligature (Wooldridge [30]), by cutting (Tigerstedt [31]), or by crushing (MacWilliam [32]), or by clamping the bundle of His (Erlanger [33]).

Erlanger has found that when the bundle of His is completely compressed by a clamp the ventricle may only respond by 1 beat to 2, and when the clamp is tightened, to 3 of the auricles.

When the clamp is still farther tightened, the 3 : 1 rhythm is succeeded by complete heart-block, so that the beats of the ventricles become completely independent of those of the auricles and usually are much slower than they. As only the bundle of His is compressed in this experiment, the blood continues to be driven into the ventricles by the auricles. They thus become distended, and after two or three waves of blood have been driven in they contract, but this contraction bears no constant time-relation to the contractions of the auricles, so that the rhythms of the auricles and ventricles are separate and independent. The ventricular rhythm is usually considerably slower than the auricular, which is on an average 3·05 times as quick.

When the bundle of His is incompletely compressed, from either imperfect application of the clamp or some other reason, the results are somewhat different. The first result of tightening the clamp may be the lengthening of the interval between the commencement of

the auricular systole and ventricular systole. For the sake of brevity the auricular systole is often denoted by the letters AS, and the ventricular by VS. This first result would thus be expressed shortly as a lengthening of the AS VS, or still more shortly, the AV interval. This interval may gradually increase until the ventricles fail to respond to one of the auricular contractions, or, in other words, an intermission occurs. Immediately after this the AV interval becomes short and then increases, at first slowly and then quickly until the next intermission. At first the intermissions occur irregularly, and with fairly long intervals, the longest being 27 beats, but as the compression increases the intermissions begin to occur regularly, the ventricle only responding to 2, 3, 4, 5, 6, 7, 8, 9, or 10 beats of the auricles.

Cause of Heart-block in Man.—It appears to be certain from numerous observations that the bundle of His does not consist entirely of undifferentiated muscle fibre, but contains numerous nerve fibres, and it is probable that communication may be maintained between the auricle and ventricle in certain cases by nerve fibres which are not contained in this bundle (Kronecker). At the same time, so many cases have been recorded where fatty degeneration of this bundle has been found on post-mortem examinations of patients who have suffered from heart-block, that there is evidently a close connection between this condition and the symptom.[34]

Functional Heart-block.—When the trunks

of the vagi are stimulated by a faradic current or the vagus centre in the medulla by digitalis, the cardiac pulsations become slower or stop altogether. These effects are due, in part at least, to heart-block (p. 68). They cease when the stimulus to the vagus trunk is discontinued, or in the case of slowing by digitalis, when the vagi are cut, so that the inhibitory stimulus can no longer pass from the medulla to the heart.

Heart-block in such cases is difficult to explain except on the hypothesis of interference (p. 36).

Nœud Vital of the Heart. Experiments of Kronecker and Schmey.—Many years ago Flourens showed that if the medulla oblongata is pricked by a needle just at the lower end of the calamus scriptorius, respiration ceases at once.[35] To this point he gave the name of nœud vital (Fig. 21). A similar point appears to exist in the heart, for Kronecker and Schmey[36] found that by puncturing a point in the septum between the ventricles, about the junction of its upper third with its lower two-thirds, the rhythmical action of the heart is stopped immediately, and as a whole it is quiescent, though little quivering tremors can be seen all over the ventricle.

In both cases the action which is abolished is an alternating one. In respiration, it is that of inspiration and expiration; in the heart, that of systole and diastole. In both cases the arrest does not seem to be due so much to paralysis as to disturbance of co-ordination between these alternating movements. Another resemblance between the nœud vital of the respiration and that

of the heart is that in neither case does the effect seem to be due to injury of ganglia. The nœud vital was investigated by Gierke,[37] who found that it practically consisted of a bundle of nerves connecting the two sides of the medulla and passing to the nuclei of the vagus and laryngeal nerves, as well as into the spinal cord. The existence of a definite centre in Kronecker's

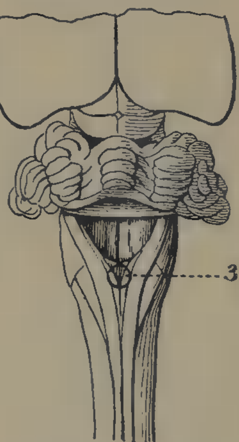


FIG. 21.—Nœud vital. The figure shows the posterior part of the cerebral hemispheres, cerebellum, and medulla oblongata in the rabbit. The small circle 3 indicates the position and size of the nœud vital. (After Flourens, *Compt. rendus*, 1858, vol. xlvii., p. 806, fig. 3.)

sense has been denied,[38] but there are numerous nerve fibres along the septum.

Fibrillation.—Fibrillary tremors are due to contraction of individual muscle cells (Fig. 18, p. 51). Though a very large number of cells may be contracting at the same time, yet as all do not contract co-ordinately, the ventricle or auricle as a whole does not contract. Fibrillation of the ventricle may be produced by:[39] (1)

puncture of the septum as above mentioned; (2) ligature of the coronary arteries; (3) embolism of the small branches of the coronary artery; (4) stimulation by powerful interrupted electrical currents; (5) by rapid cooling to 25°; (6) sometimes by rapid application of chloroform. The hearts of rabbits may sometimes recover spontaneously; those of dogs (unless very young) do not. They may sometimes be restored by very strong electric shocks of 240 volts directly to the heart.

Consequences of Fibrillation.—Fibrillation of the ventricle is fatal in a few minutes, but fibrillation of the auricle may continue for weeks or years without having any other effect than producing great irregularity of the pulse, and thus impairing the circulation.[40] When camphor is added to normal saline and blood, the mixture removes fibrillation when circulated through a heart.[41]

Extrinsic Nerves of the Heart.—The relationships between the heart and the body which it requires to supply with blood in all its parts and under varying conditions are so complicated that one would expect to find very numerous nerves connecting the body and the heart; and this is indeed the case. Around the base of the heart itself there is a large network or plexus of nerves, which for convenience of description may be divided into three parts: (1) superficial plexus; (2) right and (3) left divisions of the deep or posterior plexus. To these may be added the plexuses which accompany the anterior and posterior coronary arteries (Fig. 19, p. 54).

Nerves pass to this network from the three great cervical ganglia, and from the vagus nerve on each side. The connections of these nerves with one another and with the spinal cord are very complex, and need not be described here.[42]

Functions of these Nerves. — Speaking generally, the function of the sympathetic nerves is to quicken and strengthen the heart-beats, and they are, therefore, termed accelerating nerves.

The function of the vagus, generally speaking, is to slow the cardiac beats and render them weaker (inhibitory action).

Complex Functions of the Vagus.—This nerve has received the name of vagus or wandering nerve (in German—Herumschweifender Nerv), because it wanders to so many organs in its course; and it has also received the name of pneumogastric, because it sends a large nervous supply to the lungs and stomach as well as the intestines, liver, and kidneys. It contains three kinds of nerves: (1) medullated, with a thick medullary sheath;[43] (2) medullated, with a thin medullary sheath;[44] (3) non-medullated nerves.[43] Those of the first class are probably efferent (motor and inhibitory), those of the second are probably afferent[44] (sensory), and those of the third are sympathetic (accelerating).

Afferent and Sensory Nerves of the Heart. Pain. — The probable existence of intrinsic afferent nerves in the epicardium has already been mentioned. Afferent nerves, irritation of which will cause extra systoles followed by compensatory pauses, appear to be present also in

the pericardium, for Heitler,[45] under von Basch's direction, found that stimulation, either mechanical or electrical, of the pericardium produced extra systoles of the heart in dogs; but when the pericardium was painted with a 10 per cent. solution of cocaine, stimulation ceased to produce any result. The extrinsic afferent nerves may cause slowing or quickening of the pulse, and either a rise or fall of the blood-pressure. They produce alterations in the respiration, and may cause general reflexes of the limbs, a fact which indicates that they can produce sensation and probably pain.[46]

Depressor Nerve.—In rabbits a nerve was found by Ludwig and Cyon[47] which originates in fibres in the ventricle, passes upwards, and sends one branch to the vagus, and another to the superior laryngeal nerve. Stimulation of its peripheral end has no effect, but if the central end of the cut nerve be stimulated the blood-vessels of the intestines dilate, and the blood-pressure falls. It is sometimes present as a separate nerve in man, but appears sometimes to be amalgamated with the vagus.[48] It is not always in action, but if the pressure within the heart,[49] or perhaps rather in the aorta,[50] rises too high it comes into action, lowers the pressure, and eases the heart.

Mode of Action of the Vagus on the Heart.—When one vagus, especially the right, is stimulated, both auricles and ventricles beat more slowly and more feebly. If the stimulus is strong, they stand quite still in diastole for a variable period, after which they begin to

beat again, even though the stimulation be continued. In most animals the auricle responds more readily to vagus stimulation than the ventricle, and may stand completely still while the ventricle continues to pulsate.[51] On the other hand, the contractions of the ventricle sometimes almost disappear, while the auricles beat more strongly. When the auricle is in a state of fibrillation stimulation of the vagus may sometimes have no effect on the auricle, but may slow the ventricle or stop it altogether.[52] The exact way in which the vagus produces these extraordinary effects has given rise to much experiment, great discussion, and is not yet positively ascertained.

Some experiments appear to show that the vagus acts on the cardiac muscle directly, as a motor nerve does on voluntary muscle. Others indicate that it acts indirectly through some kind of nervous structures, and it is almost impossible to form any kind of complete conception of its mode of action unless we assume that it acts both on muscle and nerve. That it acts on muscle, appears to be indicated by the fact that it causes inhibition in the hearts of invertebrates in which no ganglion cells have been found, and also in strips cut from parts of a vertebrate heart supplied by the vagus, but containing no ganglion cells.[53]

That it acts on nervous structures as well, is indicated by the fact that it does not act at once upon the heart as a motor nerve does on a muscle, but there is a somewhat long latent period,[54] amounting often to as much as the

time of one or even two pulse-beats before stimulation produces an effect, and continues to act for a considerable time after the stimulation has ceased (Fig. 91, p. 300). Moreover, the effects of drugs on the vagus are very difficult or impossible to explain on the theory that it acts only on the heart muscle.[55]

The inhibitory fibres were shown by A. Waller to be really derived from the spinal accessory nerve, because when the roots of this nerve are torn at the jugular foramen so that it is destroyed, and its fibres degenerate, the inhibitory function of the vagus is lost, and stimulation of its trunk no longer slows the heart.[56] The deep origin of this nerve is the inhibitory centre for the heart, and is situated in the medulla oblongata.[57] In some tortoises only the right vagus has any inhibitory power;[58] and I have frequently noticed in rabbits that the inhibitory power of the right vagus is much stronger than that of the left. Branches of the right vagus go chiefly to the deep, and those from the left to the superficial cardiac plexus.

The inhibitory fibres of the vagus may (1) slow the beats of the heart without altering their strength, or (2) may weaken them without altering their rate, or (3) may both slow them and weaken them.[59] On account of sympathetic fibres being contained in the vagus trunks, stimulation of them may occasionally cause quickening and strengthening of the heart's beat instead of the usual effect.[60] Other motor fibres go to abdominal organs,[61] and probably some go to the lungs.[62] According to

Gaskell, the vagus may slow or stop the heart by depressing (1) its power of originating rhythmical stimuli; (2) of conducting them (block); (3) of responding to them (less excitability); (4) its contraction force; (5) its tonicity.[63]

Some recent investigations by A. E. Cohn[64] may help to explain why such differing results have been obtained by stimulation of the vagi. Although Gaskell and others have observed differences in the nature as well as in the amount of action exerted in the heart by stimulation of the right and left vagus, yet the differences in nature have not been explained. From a consideration of the results obtained by previous observers as well as from his own experiments, Cohn comes to the conclusion that both nerves have the double power of depressing the origination of stimuli in the heart and of lessening their conduction. The power of depressing stimuli is greater in the right vagus, whilst that of lessening conduction is greater in the left. Cohn illustrates his idea by a diagram (Fig. 22) which does not completely explain all the results, and is, therefore, imperfect, but at the same time it helps to link the facts together.

It is clear that the vagus owes its power of slowing or stopping the ventricle in part to its producing heart-block,[64] and preventing the stimuli from the auricle from passing as usual to the ventricle. Gaskell states that he has never seen any evidence that an excitation-wave (p. 32) can travel from the sinus to the ven-

tricle and cause it to contract without causing the auricle to contract.[65] Yet there are cases in which the vagus produces complete stoppage of the auricles, so that one can hardly suppose any

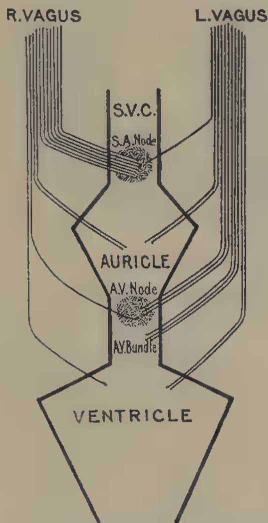


FIG. 22.—Diagram to illustrate the action of the right and left vagus on the heart of the dog. (Slightly altered from A. E. Cohn.) Speaking generally, the right vagus lessens stimuli, the left produces block. The right vagus goes chiefly to the sino-auricular node, or pacemaker of the heart, and when stimulated it stops more or less completely the origination of stimuli in the node, and thus stops the auricles, and generally the ventricles also. But if the auricles are only slowed and not stopped entirely, there was no blocking of the stimuli from them to the ventricles. The left vagus causes some slowing of the auricles, but blocks the passage of stimuli from the auricle to the ventricle. The amount of this may vary from simple prolongation of the AV time and incomplete heart-block, to complete heart-block.

stimuli are passing from them, while the ventricle continues to beat normally, or even more quickly than normally, if the accelerator nerves are stimulated at the same time as the vagus.[66]

Opposite Effects of the Vagus on Heart-

block.—Whilst the usual effect of vagus stimulation is to produce more or less complete heart-block, yet, when heart-block already exists, stimulation of the vagus will remove it. So that, in the words of Gaskell, "stimulation of the vagus will remove the block, expedite the recovery of the tissue, and cause every contraction-wave to pass."[67]

In addition to this, Gaskell states that stimulation of the vagus may, at one time, increase the force of the heart-beats and lessen it at another.[68]

Even though they should be due to two kinds of fibres in the vagus, it is not easy to understand such opposite effects except by supposing that they are caused by some kind of reinforcement and interference (Figs. 8 and 9, p. 36; *cf.* also p. 61).

The nature of such an action we do not at present understand, but neither do we know the nature of the action by which a motor nerve acts upon a muscular fibre and causes it to contract. Both actions are probably more or less chemical, and future investigations will probably explain them.

Trophic Action of the Vagus.—Gaskell considers that the function of the vagus is to build up anew those constituents of the cardiac muscle which are destroyed during contraction.[69] This idea receives confirmation from the facts that after death the heart beats longer if the vagi have previously been active, and stops sooner if the vagi had been cut.[70] * Section

* Joseph and Meltzer (*Journ. of Exp. Med.*, 1909, vol.

of the vagi during life also causes degeneration. The action of the vagus appears to depend much on its power to influence tissue change in the heart. When it is in action more potassium is given off by the heart muscle.[71] The vagus will not slow a heart perfused with a solution of sodium chloride only, but its inhibitory power returns with the addition of potassium and calcium. It is necessary for these to be in proper proportion, for if too much potassium is present the heart stands still in diastole, and if calcium is in excess it stands still in systole.[72]

Accelerating Nerves of the Heart.—The central origin of these nerves has not been determined with the same exactitude as that of the inhibitory nerves. The chief accelerating nerves appear to pass down in the cervical part of the spinal cord, and to pass from it by the rami communicantes to the first four dorsal ganglia, then upwards in the sympathetic cord through the annulus of Vieussens to the inferior cervical ganglion, and thence to the heart. There seem, however, to be other fibres which have an accelerating action. In the frog they occur entirely in the vagus, and this nerve also contains accelerating fibres in many mammals.[73] Their action is, however, masked by the more powerful inhibitory fibres, so that stimulation of the vagus trunk causes slowing of the heart unless the inhibitory fibres have been paralysed by atropine, nicotine, curare, or some poison

xi., Nos. 1 and 2) found, on the contrary, that stimulation of the vagi before or after death hastened the occurrence of rigor in the heart.

having a similar action.[74] Then vagus stimulation causes acceleration.

As the vagi have the character of spinal nerves they have a rapid effect on the heart, while the accelerating nerves belong to the sympathetic system and have a slow action. The accelerator nerves can act on the ventricle without acting on the pacemaker of the heart, for they will quicken the ventricular beats when the auricle is standing completely still from stimulation of the vagus.[75]

The accelerator nerves increase the strength as well as the rate of the heart-beats. They probably act through the ganglionic cells in the nodes. They are not directly antagonistic to the vagi. When both are stimulated, the after-result is increased cardiac efficiency.[76]

Reflex Stimulation of the Inhibitory and Accelerating Nerves of the Heart.—As the function of the heart is to supply blood to the whole body, one would naturally suppose it would respond to a call from any part of the body whatever, and this is indeed the case. Alterations in the pulse may occur from stimuli proceeding from any nerves of special sense, optic, olfactory, acoustic, or glosso-pharyngeal; from the nerves of the skin, of the muscles, or of the viscera.[77] The nature of the response depends on that of the stimulus; for, when this is slight, the accelerating nerves appear to respond to it and the pulse is quickened, but if it is great, the vagus is stimulated and the heart slowed.[78]

Reflex Stimulation of Inhibition.—Either

mechanical or electrical irritation of the pericardium [79] or of the surface of the heart will cause the ventricle to stand still. This action appears to be of a reflex nature, as it is abolished by painting with cocaine before applying the stimulus.[80] Reflex stimulation of the vagus, and stoppage of the heart occurs very readily on irritation of the mucous membrane of the nose in some animals, so that in the dog [81] and rabbit inhalation of a strong vapour of chloroform, or of ammonia, will stop the heart instantly.[82] It may occur also from other parts of the respiratory passages such as the bronchi and lungs,[83] as well as from the stomach by distension,[84] or by irritation of the mucous lining,[85] and from the intestines.[86] This latter reflex is important in relation to slowness or intermission of the heart from gastric irritation.

Reflex irritation of the vagus may indeed occur from any centripetal nerve.[87]

Valves of the Heart.—If the valves were not present, the blood, instead of being forced steadily onward by each systole of the auricles and ventricles, would tend to regurgitate, so that the heart would work at a serious disadvantage, and much of its energy would be wasted. The presence of the valves prevents this. In the aorta and pulmonary artery we have three segments, which are simply brought together like those of an ordinary pump, by the pressure within the artery when the ventricle ceases to contract. In the valves which separate the auricle from the ventricle we require something more than this, because the valves are large, and

when the walls of the ventricle approximate during systole the thin valves would be driven back into the auricle, were it not that they are attached by fine cords and by muscular columns

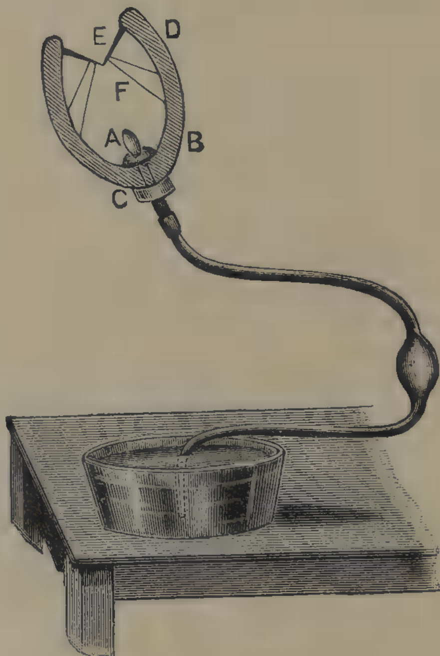


FIG. 23.—Diagram of a simple apparatus for demonstrating the action of the valves of the heart, and ascertaining their competency. It consists of an ordinary enema syringe, the nozzle of which, A, is thrust through the ventricle, B, from the inside, and kept in place by a thick rubber ring, C. D is the auriculo-ventricular ring; G, the valves; and F, the musculi papillares.

which, contracting with the rest of the ventricle, or even a little before it, draw the valves downwards and prevent them from being forced back into the auricles[88] (Fig. 23).

The action of these valves is aided by the

contraction of the muscular fibres around the auriculo-ventricular orifices, which are greatly lessened in diameter, so much so that one might say that even imperfect valves might close them (*b* and *c*, Fig. 24); whereas, when the cardiac contraction is feeble the orifices may be too large to be completely covered, and thus a certain amount of regurgitation may

Fig. 24.—(*a*) Heart fully distended, showing insufficiency of the valves to close the mitral and tricuspid orifices. (*b*) Heart in full systole, showing the mitral and tricuspid orifices so diminished by the muscular contraction that the valves close them easily. (*c*) The same heart as in *b*, from another point of view.

The casts of the heart from which the above figures are taken were made by Mr Franz Joseph Steger, 26 Talstrasse, Leipzig, and were drawn by Mr T. P. Collings, London. They were originally described by F. Hesse (*Arch. f. Anat. u. Physiol.*, *physiol. Abtg.*, 1880, p. 328).

take place even though the valves themselves are perfectly healthy (*a*, Fig. 24).[89]

The temporary mitral murmurs frequently heard in cases of cardiac weakness are probably due to this cause, and as the heart recovers strength they disappear.

Sounds of the Heart.—The closure of the valves in the heart occasions sounds which can be heard by putting the ear to the chest wall, and they can be still better localised by the use

of a stethoscope. When we do this we hear sounds which are well imitated by the syllables "lub-dup," close to one another. These syllables follow one another quickly, and then comes an interval, which represents the diastole of the heart. The credit of showing that the second sound, "dup," is caused by the closure of the aortic valves belongs to C. J. B. Williams and the committee in which he, Hale, and Glendinning took part.[90] They showed that when the aortic valves were destroyed the sound disappeared. The causation of the first sound, however, has given rise to a great deal of discussion. Some authors have considered it to be a valvular sound, and due to the flapping together of the auriculo-ventricular valves; whilst others, like Magendie, have thought it to be caused by the striking of the apex against the chest wall; and yet others have looked upon it as being a muscular sound, due to the ventricular contraction. There seems to be little doubt now, from the experiments of Ludwig, Dogiel,[91] and others, that the first sound is chiefly muscular, and brought about by the contraction of the ventricle; but the experiments of Ottomar Bayer[92] in Ludwig's laboratory demonstrated that, apart from the muscular sound, a distinct valvular click could be obtained by the closure of the auriculo-ventricular valves in a dead heart; whilst Williams and his confrères found, in addition, that the first sound was intensified by allowing the exposed heart to beat against a piece of board.[93] We may thus consider that there are

three factors which all take part in the production of the first sound, viz., (1) the ventricular contraction; (2) the closure of the auriculo-ventricular valves; and (3) the impulse of the apex against the chest wall.

As we would expect, the first sound is heard most loudly over the apex, which is the point of the chest wall nearest to the ventricle. The second sound is heard more sharply over the aortic valves, which lie beneath the left side of sternum at about the level of the third intercostal space, but is heard still better at the point where the aorta most nearly approaches the sternum at its right edge, and at the level of the second intercostal space or third costal cartilage. Gibson[94] has described a third sound occurring occasionally after the second.

Double Nature of the Heart.—For the sake of simplicity, I have to a great extent spoken of the heart as if it consisted only of the left side, but we have in man, as in other mammals, really two hearts joined together in one, the right and the left; the right sending the blood through the lungs for the purpose of aerating it, and the left sending the blood through the body in order to nourish the tissues. Both hearts receive the blood from the large veins into the auricles, which, contracting, send it on to the ventricles, and thence it is propelled by the right ventricle into the pulmonary artery, and by the left ventricle into the aorta. As I have mentioned before, both the vena cava and the pulmonary veins have the power of rhythmically independent pulsation apart from the auricle, and the

cardiac beat may sometimes, though probably not always, originate in them (p. 21).

Right Ventricle.—The resistance which the right ventricle has to overcome in driving the blood through the pulmonary artery is only about one-third that presented by the aorta, and, consequently, the right ventricle is only about one-third the strength of the left. The tricuspid valves, which separate the right ventricle from the right auricle, are much more easily rendered incompetent by distension of the ventricle than are the mitral valves, and this tendency to incompetency has been regarded, and I think with truth, as a safety-valve,[95] preventing the stoppage of the right ventricle by over-distension, and allowing the blood to pass back into the venous reservoirs, of which I have already spoken.

In cases where the arterial tension is abnormally high and the danger of cerebral hæmorrhage is consequently great, a safety-valve action sometimes occurs also in the left ventricle, which dilates, so that the mitral valves become incompetent and allow a certain amount of regurgitation to take place. This lowers the arterial tension and lessens the risk of apoplexy.

LITERATURE.

[1] Purkinje, *Breslau. Schles. Gesellsch. Uebersicht*, 1841, p. 86.

[2] Nicolai, Nagel's *Handbuch d. Physiol. d. Menschen*, vol. i., p. 801 (Braunschweig: F. Vieweg u. Sohn, 1909).

[3] Kronecker and Imchanitzky, *Archives internationales de Physiol.*, Juillet 1906, vol. iv., pp. 1-17; and pl. i.
[4] Martin Flack, "The Heart," *Farther Advances in Physiology*, edited by Leonard Hill, F.R.S., p. 38 (London: Edward Arnold, 1909).
[5] Flack, *op. cit.*, p. 45.
[6] Lee, Robert, *Phil. Trans.*, 1849, p. 47.
[7] Retzius, *Biol. Untersuch.*, New Series, vol. iii., 1892, p. 49.
[8] Ramon y Cajal, *Gaz. sanitat de Barcelona*, 10th August 1890 and 10th April 1891, quoted by Retzius.
[9] Berkeley, *The Johns Hopkins Hospital Reports*, 1894-5, vol. iv., p. 248 *et seq.*
[10] J. F. Heymans and L. Demoor, "Étude de l'Innervation du Cœur des Vertébrés," *Mémoires couronnés, par l'Académie Roy. de Médicine de Belgique*, 1894, vol. xiii., p. 10 *et seq.* and p. 48.
[11] A. Fröhlich (and von Basch), *Zentralb. f. Physiol.*, 1904, vol. xviii., p. 693.
[12] Bayliss and Starling, *Proceedings of the Royal Society*, vol. l., pp. 213 and 214.
[13] Stefani and others, quoted by Tigerstedt, *Lehrb. d. Physiol. d. Kreisl.*, p. 142 *et seq.*
[14] Ludwig and Hoffa, *Ztschr. f. rat. Med.*, 1850, p. 129; Kronecker, *Ludwig's Festgabe*, 1874, p. 191.
[15] Bowditch, *Ber. d. sächs. Gesellsch.*, 1871, p. 687, and *Ludwig's Arbeiten*, 6ter Jahrg., p. 174; Ranvier, *Leçons d'Anat. Gen.*, 1877-8, "Appareils nerv. terminaux, etc." (Paris, 1850), p. 175.
[16] Gaskell, Schäfer's *Textbook of Physiol.*, vol. ii., p. 194; *Journ. of Physiol.*, 1880, vol. iii., p. 48 *et seq.* and p. 369.
[17] Engelmann, *Pflüger's Archiv*, 1896, vol. lxii., p. 543 *et seq.*
[18] Tawara, *Reizleitungssysteme d. Saügethierherzens*, (Jena, 1906), pp. 134 and 150.
[19] Martin Flack, *op. cit.*, p. 46.
[20] Keith, *Journ. of Anat. and Phys.*, 1908, vol. xlii., p. 1.
[21] Keith and Flack, *op. cit.*, vol. xli., p. 172; *Lancet*, 11th August 1906, p. 359.
[22] Tawara, *op. cit.*, p. 134.
[23] Flack, *Farther Advances in Physiology*, p. 38.

[24] Stanley Kent, *Proc. Physiol. Soc.*, 12th November 1892, No. 6, p. 24; and *Journ. of Physiol.*, vol. xiv., 1893, p. 233.
[25] W. His, jun., *Arbeiten a. d. Med. Klinik zu Leipzig herausgegehen von Dr H. Curschmann* (Leipzig: F. C. Vogel, 1893), p. 23.
[26] Tawara, *op. cit.*, p. 134 *et seq.* and p. 150.
[27] Erlanger, *Amer. Journ. of Med. Sci.*, 1908, New Series, vol. cxxxv., p. 797.
[28] Jas. Mackenzie, *Diseases of the Heart*, p. 160 (London, 1908).
[29] A. E. Cohn, *Journ. of Exper. Med.*, 1912, vol. xvi., p. 755.
[30] Wooldridge, *Ludwig's Arbeiten*, and *Arch. f. Anat. u. Physiol.*, 1883, p. 533.
[31] Tigerstedt, *Ludwig's Arbeiten*, 1884, and *Arch. f. Anat. u. Physiol.*, 1884, p. 503.
[32] MacWilliam, *Journ. of Physiol.*, 1886, vol. ix., p. 177.
[33] Joseph Erlanger, *Journ. of Exper. Med.*, vol. viii., p. 13 (New York, 1906).
[34] Lewis, *Mechanism of the Heart Beat*, pp. 97-112 (London, 1911).
[35] Flourens, *Compt. rend.*, 1858, tom. 47, p. 813; and *Recherches experiment s. les Proprietés et Fonctions du Système Nerveux*, 2nd edition, p. 201 (Paris, 1842).
[36] Kronecker and Schmey, *Sitzungsb., d. Akad. d. Wiss. zu Berlin*, 1884, p. 87.
[37] Gierke, *Arch. f. Anat. u. Physiol.*, 1873, vol. vii., p. 583.
[38] MacWilliam, *Journ. of Physiol.*, 1887, vol. viii., p. 300.
[39] See literature in F. B. Hofmann's article in *Nagel's Handb. d. Physiol. d. Menschen*, Bd. i., p. 239 (Braunschweig, 1909).
[40] Lewis, *Mechanism of the Heart Beat*, p. 229 (London, 1911).
[41] Meyer and Gottlieb, *Exper. Pharmacologie*, p. 217 (Berlin u. Wien, 1910).
[42] *Vide* Tigerstedt, *Lehrb. d. Physiol. d. Kreisl.*, p. 228; Gibson, *Nervous Affections of the Heart*, p. 24 *et seq.* (Pentland: London and Edinburgh, 1904); A. Morison, *Nervous Systems and Visceral Disease* (Pentland: London and Edinburgh, 1899); Wool-

dridge, *Ludwig's Arbeiten*, 1883, and *Arch. f. Anat. u. Physiol.*, 1883, p. 524.

43 Gaskell in Schäfer's *Textbook of Physiol.*, vol. ii., p. 200.

44 Schweigger, Seidel, *Unpublished Notes of Lectures given in Ludwig's Laboratory in Summer of* 1869.

45 Heitler, *Wiener klin. Wochenschr.*, 1898.

46 Goltz, *Centralb. d. med. Wiss.*, 1863, pp. 17, 497, and *Virch. Arch.*, vol. xx., p. 10 *et seq.;* Budge, *Arch. f. Physiol. Heilk.*, 1846, vol. v., p. 588; Gurboki, *Pflüger's Arch.*, 1872, vol. v., p. 289; Wooldridge, *Ludwig's Arbeiten*, 1883, and *Arch. f. Anat. u. Physiol.*, 1883, p. 522 *et seq.*

47 Ludwig and Cyon, *Ludwig's Arbeiten* for 1866, p. 128.

48 *Vide* Hill, Schäfer's *Textbook of Physiol.*, vol. ii., pp. 59 and 60; and Tigerstedt, *op. cit.*, p. 279.

49 Sewall and Steiner, *Journ. of Physiol.*, 1885, vol. vi., p. 174.

50 Köster and Tschermak, quoted by Hofmann, *Nagel's Handbuch d. Physiol.*, Bd. i., p. 283.

51 Variations occur, and these are described and literature given by Tigerstedt, *op. cit.*, p. 247.

52 F. Franck, *Archiv d. Physiol.*, 1891, p. 583, Kronecker.

53 *Vide* Tigerstedt, *op. cit.*, p. 253 *et seq.*

54 Donders, *Pflüger's Archiv*, 1868, vol. i., 338 *et seq.*, and 1872, vol. v., p. 6.

55 Schmiedeberg, *Grundriss d. Pharmacologie*, p. 137 (Leipzig: Vogel, 1902).

56 A. Waller, *Gaz. méd. de Paris*, 1856, p. 420.

57 *Vide* F. Hofmann in *Nagel's Handb. d. Physiol.*, Bd. i., p. 276.

58 A. B. Meyer, *Das Hemmungsnervensystem des Herzens*, p. 60.

59 Gaskell, *Proc. Roy. Soc.*, 1881, vol. xxxiii., p. 201; Schmiedeberg, *Ludwig's Arbeiten*, 6ter Jahrg. for 1871, p. 34 *et seq.* (Leipzig: Hirzel, 1872), and *Sitzungsb. d. k. säch. Gesellsch. d. Wiss.*, vol. xxiii., p. 148 *et seq.*

60 Gaskell, *Journ. of Physiol.*, 1884, vol. v., p. 46.

61 Hermann's *Handbuch d. Physiol.*, vol. v., part 2, pp. 444 and 450.

62 *Ibid.*, vol. iv., part 2, p. 243.

[63] Gaskell, Schäfer's *Textbook of Physiol.*, vol. ii., p. 209.
[64] A. E. Cohn, *Journ. of Exp. Med.* 1912, vol. xvi., p. 732; *vide* also Kraus and Nicolai, *Das Electrokardiogramm*, p. 147 (Leipzig: Veit & Co., 1910).
[65] Gaskell, *Journ. of Physiol.*, 1882, vol. iii., p. 376.
[66] Bayliss and Starling, *Journ. of Physiol.*, 1892, vol. xiii., p. 414.
[67] Gaskell, *Journ. of Physiol.*, 1882, vol. iii., p. 377.
[68] Gaskell, *Proc. Roy. Soc.*, 1881, vol. xxxiii., p. 203.
[69] Gaskell, *Journ. of Physiol.*, 1886, vol. vii., p. 50.
[70] Brown-Séquard and others, quoted by Tigerstedt, *op. cit.*, p. 258 *et seq.;* Traube, *Gesammelte Beiträge*, vol. i., p. 381 (Berlin, 1871); Eichhorst, *Die trophischen Beziehungen der Nervi Vagi zum Herzmuskel*, p. 18 (Berlin, 1879); Wassilieft, *Zeitschr. f. Klin. Med.*, 1881, vol. iii., p. 316.
[71] Howell and Duke, *Amer. Journ. of Physiol.*, 1908, vol. xxi., p. 51.
[72] *Vide* Meyer and Gottlieb's *Pharmacologie*, p. 229.
[73] *Vide* Tigerstedt, *op. cit.*, p. 260 *et seq.*
[74] Rutherford, *Journ. of Anat. and Physiol.*, 1869, vol. iii., p. 408; Boehm, *Arch. f. exp. Path. u. Pharm.*, 1875, vol. iv., p. 363; Dale, Laidlaw, and Symons, *Journ. of Physiol.*, 1910, vol. xli., p. 1 *et seq.*
[75] Bayliss and Starling, *Journ. of Physiol.*, 1892, vol. xiii., p. 414.
[76] Tigerstedt, *op. cit.*, p. 272.
[77] Tigerstedt, *op. cit.*, p. 289.
[78] Simanowsky, quoted by Tigerstedt, *op. cit.*, p. 288.
[79] Heitler, *Wiener klin. Wochenschr.*, 1898.
[80] A. Fröhlich and von Basch, *Zentralb. f. Physiol.*, 1904, vol. xviii., p. 693.
[81] François Franck, *Trav. de Laboratoire de Marey*, 1876, vol. ii., p. 226.
[82] Lauder Brunton, "Experiments," *vide* "Shock and Syncope," *Practitioner*, 1873, vol. xi., p. 246; also Kratschmer, *Wiener Sitzungsb.*, 1870, vol. lxii., p. 24.
[83] François Franck, *op. cit.*, 1880, vol. iv., p. 378.
[84] Mayer and Pribram, *Sitzungsb. d. k. Akad. d. Wiss. Math. Nat. Cl.*, 1872, vol. lxvi., p. 102.
[85] Hermann and Ganz, *Pflüger's Archiv*, 1870, Bd. iii., p. 8.
[86] Tigerstedt, *op. cit.*, p. 282 *et seq.*, and p. 289.

[87] Tigerstedt, *op. cit.*, p. 289.
[88] Lauder Brunton, *St Bartholomew's Hospital Reports*, 1878, vol. xv., p. 283.
[89] Ludwig and Hesse, *Arch. f. Anat. u. Physiol.*, 1880, *Anat. Abtg.*, p. 344; Macalister, *Brit. Med. Journ.*, 28th October 1882, p. 825.
[90] *Sixth Report of the British Association*, 1836, p. 265.
[91] *Ludwig's Arbeiten*, 1878, p. 78.
[92] O. Bayer, *Arch. f. Heilk.*, 1870, vol. xi., p. 157.
[93] *Report of the Fifth Meeting of the British Association*, 1835, p. 246.
[94] Gibson, *Lancet*, 1907, vol. ii., p. 1380.
[95] Wilkinson, *Guy's Hospital Report*, 1837, p. 132.

CHAPTER IV

PHYSIOLOGY OF VESSELS: BLOOD-PRESSURE

Aorta—Arteries, Arterioles and Capillaries—Vaso-motor Nerves—Dilating Nerves—Elongation of Muscle (?)—Contraction of Veins—Rhythmical Contraction of Vessels—Stimulation of Blood-vessels from without—Stimulation from within—Internal Secretions—Toxins—Double Function of the Kidney—Effect of Heat and Cold on the Systemic Circulation—Fever—Effect of Heat and Cold on the Pulmonary Circulation—Blood-pressure—Schema of the Circulation—Kymographs—Blood-pressure in Animals—In Man.

Aorta.—On looking at the aorta, one would say that it is entirely composed of fibrous tissue, and consequently is not likely to possess any contractile power; and yet it would appear to have such a power, for in the case of a criminal executed by decapitation at Würzburg, it was found to contract on the application of electricity shortly after death.[1]

Arteries and Capillaries.—As we pass down the arterial system the muscular fibres become more developed, and in the arterioles we find a continuous muscular layer, while in the capillaries we have nothing but contractile cells. Just as in the case of the heart, where we have

two kinds of nerves having an opposing action, so we have in the vessels, nerves which cause contraction, and others which cause dilatation. When working with Schweigger-Seidel in Ludwig's laboratory in 1869, I made a number of observations on the nerves of the arterioles and veins, but these were not published, as I did not discover anything new. I tried in vain to find any evidence of nerve fibres entering the muscular cells of the arterioles, but could never observe it. All that I could find was a regular network of minute nervous fibrils running over the surface of the muscular layer. At the points

FIG. 25.—Diagram of the nerve fibrils, ramifying like a net over the muscular layer of an arteriole.

where these fibrils cross there are small thickenings or knots, but nothing at all like ganglion cells (Fig. 25). The same has been observed by Heymans and Demoor in the apex of the rabbit's[2] heart and in the coronary arteries.

Vaso-motor Nerves. Dilating Nerves. Elongation of Muscle (?).—The vaso-motor system, as I have already said, has its chief centre in the medulla oblongata, but it has subsidiary centres in the spinal cord itself, and in the ganglionic chain of the sympathetic. When the vaso-motor centres or the trunks of the vaso-motor nerves are irritated, the vessels contract;

but there are other nerves which, when irritated, cause dilatation instead of contraction, and this dilatation is greater than that which occurs on the division of the vaso-motor fibres supplying the vessel.[3] This fact is generally explained by supposing that irritation of the dilating nerves has an inhibitory action upon local vaso-motor mechanisms close to the vessels; though, for my own part, I should be inclined to accept the

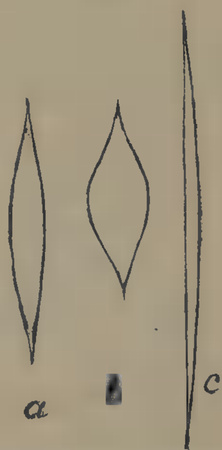


FIG. 26.—Diagram to illustrate the hypothetical transverse contraction of muscle. (*a*) Muscle in relaxed condition, (*b*) in contraction, (*c*) in elongation.

much simpler explanation that a transverse as well as a longitudinal contraction may occur in the muscular cells of the arterioles, and such a transverse contraction would elongate each cell, and dilate the vessel just as the longitudinal contraction would shorten and thicken the cell, and thus contract the vessel (Fig. 26). In many instances, dilatation or dilation is connected

with peripheral ganglia—for example, in the sub-maxillary gland, and in the nervi erigentes—but that it is always due to such nervous causation is, I think, doubtful. For a good while the contractility of capillaries was doubted, but the observations of Stricker and others have now, I think, put this fact beyond dispute.[4] When working under Ludwig's direction I also noticed that local irritation would sometimes cause, not contraction, but dilatation of an arteriole.[5] Similar observations were made by Gunning and Cohnheim in the frog; so that, just as the effect of nerves upon the heart itself, to the exclusion of muscular irritability, is now recognised to be wrong, so in all probability the properties of the muscular elements of the arterioles, like those of the heart, will by and by receive more attention than they have hitherto done.

Contraction of Veins.—By looking at the back of the hand, anyone can observe what great differences occur from time to time in the size of the veins. The dependence of venous contraction upon vaso-motor nerves was shown by Mall in Ludwig's laboratory.[6] He found that irritation of the splanchnic nerves caused the exposed portal vein to contract so forcibly, that when the irritation was long continued the lumen of the vein was quite abolished. Irritation of the sciatic causes the superficial veins of the hind legs to contract in animals.[7] Adrenin applied to ring preparations of peripheral veins causes them to contract in the same way as arteries, and when applied to rings from the

superior cava near the heart, causes them to beat rhythmically.[8]

Rhythmical Contraction of Vessels.—Rhythmical contraction of the veins was observed to exist by Wharton Jones,[9] Schiff,[10] and Vulpian.[11] The arteries also contract rhythmically under the influence of the vaso-motor centre, and give rise to periodic pulsations which are coincident with respiration. In addition to these, however, the arteries themselves pulsate[12] periodically.[13] It is difficult to see this pulsation in healthy people, but it can be well observed, as a rule, in patients suffering from aortic regurgitation. In such cases the face is usually pale, but if the finger-nail be rapidly drawn across the forehead, a red streak appears which alternately widens and narrows, and this movement on careful observation will be seen to show three rhythms. The first coincides with the pulse, and occurs about 60 to 80 times per minute; the second with respiration, about 18 or 20 times; and the third, or capillary rhythm, about three times per minute,[14] or once in 20 seconds. Douglas Cow has observed rhythmical contraction[15] in strips of vessels treated with ergot and adrenalin. The average time was 25 seconds. I have myself felt a similar rhythm in the radial artery with a cycle of 20 pulsations or 3 to 4 per minute.

Stimulation of Blood-vessels from without.—It is difficult to explain the various local alterations of the circulation, if we look entirely to the nervous system for an explanation of them; whereas the explanation is easy if we acknowledge the power of vessels to contract,

or dilate from alterations in their contractile element apart from the nervous; although, just as in the heart, we must fully recognise the enormous influence of the nervous system upon the vessels. Thus, when we apply a mustard poultice to the skin, the rapid dilatation of the vessels and consequent redness which immediately follows the application are probably due to nervous influence. In this case the nervous plexus (Fig. 25) seems to act as a reflex centre for dilatation of the vessels, although it contains no ganglionic cells. The permanent redness, which may remain for several days, is more likely to be due to a local alteration in the vessels themselves (Ninian Bruce).[16]

Stimulation of Vessels from within.—A still more important question, however, than the effect of irritation of the vessels from the outside, is that of stimulation from the inside by various products of glandular secretion, or tissue waste, or by strain.

Internal Secretions.—The first discovery of internal secretion was made by Claude Bernard, in the case of the liver, which, as he found, poured out bile into the bowel (external secretion) and sugar into the blood (internal secretion).[17] Of late years it has been found that several glands which have no external secretion at all have internal secretions of the greatest physiological importance, and some of these play a great part in regulating the contraction of the capillaries and maintaining the blood-pressure at a proper height.[18] Thyroid gland or its extract when taken by the mouth

dilates the peripheral vessels, makes the skin warm and moist, and quickens the pulse.[19] The suprarenal and pituitary bodies and their extracts have an action opposite to the thyroid.[20] It is supposed that they constantly pour these secretions into the circulation,[21] and thus maintain the arterial tension. When the medullary part of the suprarenal gland is diseased, the heart becomes feeble,[22] the blood-pressure low, and the digestion weak; whilst if the cortex also is diseased the peculiar bronzing of the skin also appears, and completes the picture of Addison's disease.[23] Extract of the cortex of suprarenal glands when injected directly into the circulation causes stimulation of the heart and great contraction of the arterioles, so that the blood-pressure rises enormously.[24] This rise only lasts a short time, but may be renewed by a fresh injection. In life the gland probably secretes slowly but continuously, so that the tension is maintained without rising too high. The pituitary body consists of three parts, of which the intermediate one appears to secrete substances which have a mixed action, some of them causing contraction of the blood-vessels in the general circulation, but dilating those of the kidney, and producing diuresis. Others cause contraction of the renal vessels, and lessen the urinary secretion.[25]

Toxins.—Substances having a similar action to suprarenal extract, but more prolonged, have been made synthetically. They all belong to the class of amines or ammonias in which hydrogen is replaced by an organic radical.[26]

Two such amines have been obtained from putrid meat, and also when bacilli from human fæces are added to broth containing tyrosin, which is one of the products of pancreatic digestion.[27]

Double Function of the Kidney.—In addition to its power of secreting urine, it is probable that it has an internal secretion also.[28] It has, moreover, very considerable metabolic power, for Schmiedeberg found that if blood containing benzoic acid is circulated through an excised kidney the urine secreted contains hippuric acid.[29] It is possible that the rise of blood-pressure in nephritis is due either to some alteration of metabolic power,* or else to lessened power to excrete the substances which tend to raise the tension. Extract of kidney itself seems to raise the tension somewhat when injected into animals,[30] but this effect is much more marked when one or both kidneys have been removed, so that excretion of the tension-raising substances is prevented.[31] In persons suffering from renal disease [32] removal of portions of the kidney causes a rise of blood-pressure in animals without the injection of any kidney-extract.[33] In renal disease it varies inversely as the extent of kidney present.

Probably the loss of some metabolic or excretory power, due to shrinking of the renal cortex

* Jaarsveld and Stokvis found (*Arch. f. exp. Path. u. Pharm.*, 1879, vol. x., p. 295) that hippuric acid may undergo conversion into benzoic acid in the body of some animals and of persons suffering from renal disease.

in chronic interstitial nephritis, is the cause of the gradual rise of blood-pressure in this disease. It often rises so high as to threaten life, either from cardiac failure or from arterial rupture. This high tension appears to commence by increased resistance to the passage of blood through the arterioles and capillaries. By some it is attributed to chronic contraction of the arterioles with hypertrophy of their muscular walls,[34] by others to a fibroid thickening.[35] It is probable that both of these conditions occur, but for my own part I am inclined to believe that the arterial contraction plays a very great part in it, as we are able in very many cases to reduce the tension by means of appropriate medicines, such as nitrites, which one would hardly do if it were entirely or even mainly due to a fibroid condition. This view also enables us to understand why nitrites sometimes fail to act, for if the high tension is due to much fibrosis and little spasm they cannot lower the tension. High tension due to toxic substances reacts on the vessels and may produce atheroma in them, so that ultimately functional contraction becomes complicated by organic change.[36]

Effect of Heat and Cold on the Circulation.—Two agents which have a very marked effect, both upon the vessels and the heart, as well as on muscular tissue generally, are heat and cold. When we put the hand into hot water we find at once that the arteries dilate and the hand becomes red, showing that the capillary circulation is free; but we notice also that the veins not only become full, but become lighter in

colour, evidencing that the blood within them is more arterial. Heat applied to the heart quickens its pulsations,[37] and at the same time increases their strength, the quickening being chiefly due to the effect of the heat upon the sinus or auricles, and the increased strength to its effect upon the ventricle.[38] Cold has an opposite effect. When applied to the extremities, it makes the arteries contract, the fingers shrink and become pale, though after a while the veins appear to dilate, and the skin assumes a bluish colour from venous congestion. Cold applied to the heart makes its movements both slower and feebler.

It is evident from what I have said that the local action of either heat or cold upon the vessels and heart is of such a character as in itself to co-ordinate the effect it produces upon both, independently of a nervous system, if applied to both at the same time; because when heat causes the vessels to dilate, so that a larger supply of blood is demanded, it also causes the heart to pulsate more quickly and more forcibly, so as to give the necessary supply. When the arteries are contracted by cold and a small amount of blood only can pass through them, the cold acts on the heart also, slowing and weakening its contraction, and thus lessening the supply. But while cold and heat may act nearly equally upon the extremities and the heart of a frog, it is not so in warm-blooded animals, where the temperature of the interior of the body remains nearly the same, notwithstanding the extremes of heat and cold

to which the extremities may be subjected, and in them it is necessary to have a nervous system to regulate the pressure of blood.

Fever.—In fever the increased temperature of the body stimulates the heart and dilates the vessels, so that the pulse is quickened in a twofold fashion.

Effect of Heat and Cold on Pulmonary Capillaries.—I have found that if a stream of warm moist air be first directed on the lung of a frog, and immediately afterwards a stream of cold moist air, the capillaries sometimes contract as much as one-third of their diameter under the influence of the cold.[39] This reaction may explain the feeling of constriction in the chest which sometimes comes on when passing from a warm room into cold air, and also the action of a wind in the face, causing angina pectoris.

Blood-pressure. Schema.—A very simple schema of the circulation which is useful in obtaining a thorough comprehension of its mechanism can easily be made by anyone. It consists of an india-rubber ball representing a heart, an elastic bulb representing the arteries, a soft-walled bag representing the veins. By connecting this with a mercurial manometer, such as that of an ordinary sphygmomanometer, the comparative effects of the heart and vessels upon the pressure in the arterial system can be readily observed. The soft-walled bag, or veins, can contain all the fluid in the whole vascular system, or even more. In using this schema we commence with the pressure at zero, and slowly

compress the india-rubber ball, representing the heart. As it is emptied it drives the fluid into the elastic bulb, or arterial system. If the passage is left open into the venous bag, the mercurial column oscillates with each pulse, rising as the fluid is driven in, and sinking

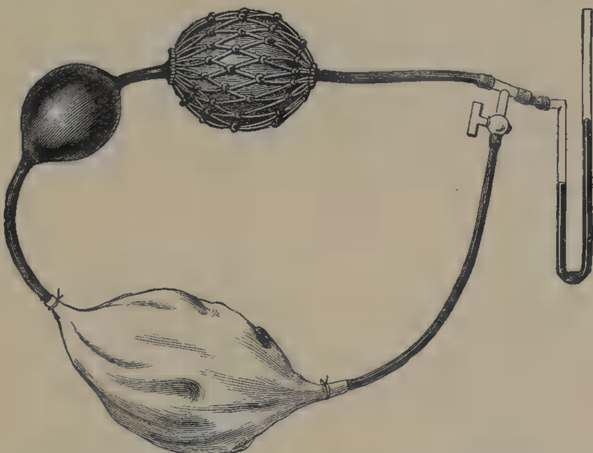


FIG. 27.—Simple schema of the circulation. It consists of a spray-producer, bladder, and mercurial manometer. The elastic ball of the spray-producer represents the heart, the elastic bag, covered with netting to prevent too great distension, represents the aorta and arterial system, and the bladder represents the venous system.

again in the interval. But if the stopcock is turned so as to prevent all the fluid driven in at each pulsation from going into the veins, the pressure will gradually rise in the bulb until it is sufficient to drive out during the diastole all the fluid sent in during the systole.

Kymographs.—The pressure is measured in animals by putting a cannula into an artery and connecting it with a mercurial manometer.[40] In

order to prevent coagulation, the tube leading from the artery to the manometer is filled either with some saline solution or solution of peptone,[41] which hinders coagulation, or leech-extract (hirudin)[42] is injected. The oscillations of the mercurial column are recorded on a revolving cylinder, and the whole instrument, consisting of mercurial manometer and recording cylinder, is called Ludwig's kymograph.

In order to avoid the intrinsic oscillations of a mercurial column other recording instruments have been employed, such as the spring manometer of Fick, in which the tension causes a curved tube to straighten or bend, or the manometers of Hürthle or Roy, where the oscillations are very small, but are much magnified by the recording lever.

Blood-pressure in Animals.—The average blood-pressure in animals varies according to their size, but not to the extent that we should imagine. In a horse it has been found to be roughly between 200 and 300 mm., in a dog 140 to 170, in a sheep 150 to 170.[43]

Blood-pressure in Man.—In man it has been found to be from 100 to 160, in cases where it was estimated in a limb before amputation.[44]

LITERATURE.

1 *Verhandl. d. Med. Phys. Gesellsch.*, Würzburg, 1854, p. 1, quoted in Schmidt's *Jahrb.*, vol. lxxxv., p. 12.

2 "Études de l'Innervation du Cœur, etc.," par J. F. Heymans and L. Demoor, *Mémoires Coronnés Acad.*

Roy. de Méd. de Belgique, 1894, vol. xiii., pl. xviii., fig. 34.
[3] *Vide* Tigerstedt, *Lehrb. d. Physiol. d. Kreisl.*, p. 512 (Leipzig: Veit & Co., 1893).
[4] Stricker, *Sitzungsb. d. k. Akad. d. Wiss. Math. Nat. Cl.*, 1865, vol. xli., Abt. 2-3; 1866, vol. li.; 1876, vol. lxxiii., Abt. 3, p. 316.
[5] Lauder Brunton, *Ludwig's Arbeiten*, 4ter Jahrg.; and *Collected Papers on Circulation*, First Series, pp. 160, 178.
[6] Mall, *Ludwig's Arbeiten*, 1890.
[7] Thompson, *Arch. f. Anat. u. Physiol.*, 1893, p. 102; Bancroft, *Amer. Journ. of Physiol.*, 1898, vol. i., p. 477.
[8] Russell Wells and Leonard Hill, *Proc. Roy. Soc.*, 1913, p. 192.
[9] Wharton Jones, *Phil. Trans.*, 1852, p. 131.
[10] Schiff, *Arch. f. Physiol. Heilk.*, 1854, vol. xiii., p. 523.
[11] Vulpian, *Compt. rend. d. Soc. Biol.*, 1856, vol. iii., p. 183; 1858, p. 3.
[12] Schiff, *Arch. f. Physiol. Heilk.*, 1854, vol. xiii., p. 524.
[13] Lauder Brunton, *Ludwig's Arbeiten*, 4ter Jahrg., 1869, p. 106.
[14] Lauder Brunton, *Journ. of Physiol.*, 1884, vol. v., p. 14.
[15] Douglas Cow, *Journ. of Physiol.*, 1911, vol. xlii., p. 141.
[16] Ninian Bruce, *Arch. f. exp. Path. u. Pharm.*, 1910, vol. lxiii., p. 424.
[17] Claude Bernard, *Leçons de Physiologie exp.*, vol. i., p. 31 *et seq.* (Paris, 1855).
[18] A very complete account, with full bibliography, is given by Swale Vincent, *Ergebnisse d. Physiol.*, 9 Jahrg., 1910, p. 451 *et seq.* (Weisbaden: Bergmann).
[19] Lauder Brunton, *St Bartholomew's Hospital Journal*, December 1897.
[20] Oliver and Schäfer, *Journ. of Physiol.*, 1895, vol. xviii., p. 278; Howell, *Journ. of Exp. Med.*, 1898, vol. iii., p. 245 *et seq.*; Schäfer and Herring, *Phil. Trans.*, 1906, B., vol. cxcix., p. 27.
[21] Ehrmann, *Arch. f. exper. Path. u. Pharm.*, 1905, vol. liii., p. 110; Strehl and Weiss, *Pflüger's Archiv*, 1901, vol lxxxvi., p. 107.
[22] *Cf.* Oliver and Schäfer, *Journ. of Physiol.*, 1895, vol. xviii., p. 269; gives literature also.

[23] Gibson, *Brit. Med. Journ.*, 27th July 1912, p. 167.
[24] Oliver and Schäfer, *Journ. of Physiol.*, 1895, vol. xviii., p. 239.
[25] Oliver and Schäfer, *op. cit.*, vol. xviii., p. 277; W. H. Howell, *Journ. of Exp. Med.*, 1898, vol. iii., p. 245 *et seq.*; Schäfer, *Proc. Roy. Soc.*, 1909, B., vol. lxxxi., p. 442 *et seq.*, with bibliography.
[26] Dixon and Dale, *Brit. Med. Journ.*, 7th August 1909, vol. ii., p. 329; and *Journ. of Physiol.*, 1909, vol. xxxix., p. 25.
[27] Barger and Walpole, *Journ. of Physiol.*, 1909, vol. xxxviii., p. 350.
[28] Brown-Séquard, *Compt. rend.*, 1892; Brown-Séquard and d'Arsonval, *Compt. rend.*, 1892, tom. 114, p. 1399, and *Arch. de Physiol.*, 1893, p. 200; E. Meyer, *Arch. de Physiol.*, 1893, p. 761, and *ibid.*, 1894, p. 179; Tigerstedt and Bergmann, *Trans. of XIIth Congress of Medicine*, Moscow, 1897, section of Physiology, p. 24.
[29] Bunge and Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, vol. vi., p. 233; Schmiedeberg, *ibid.*, vol. xiv., p. 379.
[30] Cromaine, *Recherches exp. s. l. sécretion interne des reins*, Thesis (Nancy, 1902); quoted by Parisot, *Secretion interne et pression arterielle*, p. 295 (Paris, 1908).
[31] Parisot, *op. cit.*, p. 298.
[32] Parisot, *op. cit.*, p. 302.
[33] J. Rose Bradford, *Allbutt's System of Medicine*, 1st ed., vol. iii., p. 335; 2nd ed., 1908, vol. iv., part 1, p. 583.
[34] Geo. Johnson, *Brit. Med. Journ.*, 1873, vol. i., p. 59.
[35] Gull and Sutton, *Trans. Path. Soc.*, London, 1877, p. 361.
[36] Rickett, *Journ. of Path. and Bacteriology*, 1908, vol. xii., p. 15 *et seq.*
[37] Lauder Brunton, *St Bartholomew's Hospital Reports*, 1871, vol. vii., p. 216 *et seq.*; and *Collected Papers*, First Series, p. 204. The earlier literature is here given.
[38] Gaskell, *Phil. Trans.*, 1882, p. 993.
[39] Lauder Brunton, *Brit. Med. Journ.*, 1875, vol. i., p. 201; and *Collected Papers*, First Series, p. 333.

[40] The technique is described in my *Collected Papers*, First Series, p. 279 *et seq.*

[41] Schmidt-Mühlheim, *Arch. f. Anat. u. Physiol.*, Leipzig, 1880, p. 33; and *Ludwig's Arbeiten* for 1880, p. 50.

[42] Haycraft, *Proc. Roy. Soc.*, 1884, vol. xxxvi., p. 478.

[43] Tigerstedt, *Lehrb. d. Phys. d. Kreisl.*, p. 328.

[44] Faivre, and also Albert, quoted by Tigerstedt, *op. cit.*, p. 329.

CHAPTER V

EXAMINATION OF BLOOD-PRESSURE IN MAN

Measurement of Blood-pressure in Man—Instruments—Sphygmomanometers — Bulb forms — Band forms —Standardisation of Aneroids—Method of using Bulb Sphygmomanometers—Fallacies—Use of Band Sphygmomanometers—Fallacies—Systolic Pressure —Effect of Food—Effects of Exercise—Effect of Emotion — Diastolic Pressure — Measurement of Diastolic Pressure — Instruments — Relations of Systolic to Diastolic Pressure—Pulse Pressure—Significance of Pulse Pressure—Size of Vessels—Measurement of Pressure in Veins—Measurement of Pressure in Capillaries.

Measurement of the Blood-pressure in Man.—It is naturally of very great importance that we should be able to estimate the pressure in man without opening an artery, and numerous instruments have been devised for this purpose.

By simply feeling the pulse with a finger, one can roughly make out whether the pressure within it is high or low, and this is still better done by placing three fingers upon the pulse and compressing it with the one nearest the heart, and noticing with the middle one when it ceases to beat. By the amount of pressure

exercised one can form some judgment regarding the tension, but it is evident that one cannot convey any quantitative knowledge regarding the pulse felt this way to another. The third finger nearest the hand compresses the artery so as to obstruct the recurrent pulse from blood flowing through the ulnar artery and palmar arch.

Instruments.

The first man to invent a practical sphygmomanometer for clinical use was von Basch. Instead of compressing an artery by a finger alone, he placed beneath the finger a caoutchouc bulb filled with air, and connected with an aneroid manometer in which the amount of compression could be read off. He showed that this instrument correctly indicated the pressure within the compressed vessel, by connecting one femoral artery of a dog with a mercurial manometer and compressing the other by an elastic bulb. When the pressure inside the bulb was gradually raised it was found that the pressure which stopped pulsation in the distal part of the artery was the same as that indicated within the other artery by the manometer.[1]

Sphygmomanometers. — These may be roughly divided into two classes. Those that compress a single artery and those which compress a digit or limb. Those which compress a single artery consist of an india-rubber bulb connected with a measuring apparatus like that of von Basch. The best known of them are

von Basch's,[2] Potain's,[3] Oliver's,[4] Hill's,[5] and Sahli's.[6] The advantage of these instruments is that they can be applied quickly and easily, so that in cases of nervous and troublesome patients they can be used when a band instrument would not be tolerated. Their disadvantage is that unless they are most carefully applied they are less accurate. Different observers using the same instrument may obtain readings differing as much as 20 mm. or even more, so that when a really accurate estimate is required in a patient I think a band instrument should be used.

Bulb Sphygmomanometers. — Von Basch's consists of an india-rubber bulb filled with air, and communicating with a manometer, mercurial or aneroid. The bulb is placed over an artery, generally the radial, and pressed down on the artery till the pulse beyond can no longer be felt. The pressure required to stop the pulse is then read off on this manometer. Potain's instrument differs from von Basch's only in the bulb having thinner rubber on the side to be laid on the artery, and thicker rubber on the other sides.

Oliver's first sphygmometer consists of a bulb filled, not with air but with glycerine. On this a rod rests, which communicates the pressure by means of a spring to an index moving on a dial. Leonard Hill's consists of a small, very flat funnel with a graduated stem. The wide end of the funnel is closed by a membrane and the small end by a stopcock. In this is a coloured fluid, which works against the resistance of the enclosed air. Sahli's is like von Basch's, but

has a larger bulb and a very portable mercurial manometer.

Band Sphygmomanometers. — The second class of sphygmomanometers are those which compress the arm or finger. Gaertner's tonometer, which compresses the finger, is much used in Germany, but is not often employed in this country.[7]

It consists of a metal ring (A, Fig. 28) 1·5 cm. broad, to the inside of which an india-rubber membrane is fixed, so as to leave an air space between it and the ring. This space communicates by an opening in the side of the ring, and a T-tube with a manometer and a pressure-ball. The ring is placed loosely on the middle phalanx of one finger, and the blood pressed out of the last phalanx, either by rolling a thick, narrow india-rubber ring upwards, or by wrapping a piece of fine india-rubber tubing tightly round the finger from its tip upwards (B, Fig. 28). The pressure is then raised in the apparatus to a point which is certain to be above the pressure in the arteries, *e.g.* 200 mm. of mercury. The india-rubber ring is then rolled off or the tube unwound, leaving the last phalanx white and bloodless. The pressure is then lessened and the finger-tip watched, so as carefully to note when it begins to flush with the returning circulation. The height of the mercurial column at this moment indicates the systolic pressure in the digital arteries.

The instruments which compress the arm consist of a flat india-rubber bag, the outside of which is covered with some unyielding substance,

and is connected both with a bulb, which can be used to inflate it, and with a measuring apparatus, which may be either a mercurial column or an aneroid. This bag is strapped on the arm and

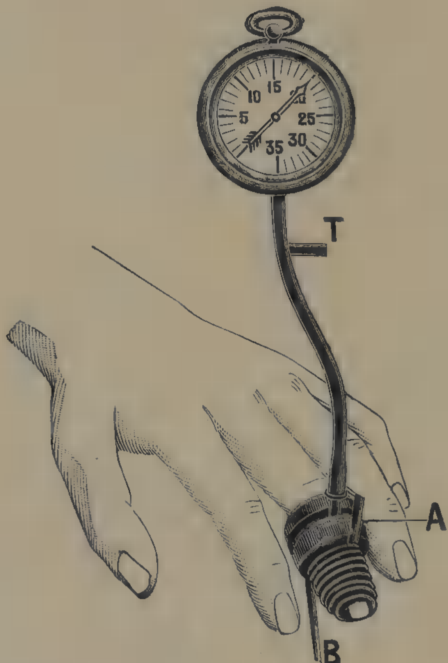


FIG. 28.—Gaertner's portable tonometer; A is a metal ring with india-rubber membrane inside. B is a piece of india-rubber tubing wound round the end of the finger so as to drive all the blood out of it. T is a tube communicating with a pressure-bulb.

gradually inflated until the pressure is sufficient to stop the pulse at the wrist. The pressure is then read off on the mercurial column or the aneroid. This method was introduced independently by Riva Rocci,[8] and by Hill and Barnard.[9]

I think the best single instrument for applying it is Martin's non-spillable mercurial sphygmomanometer.[10] An aneroid can also be used with this bag, and is more convenient for carrying about, as the aneroid, the bulb to increase the pressure, and the armlet can all be conveniently carried in the pocket.[11] By the arrangement shown in Fig. 29 either a bulb

FIG. 29.—Author's apparatus for using a broad Riva-Rocci band with von Basch's or Potain's sphygmomanometer instead of a mercurial manometer.

or an armlet can be used at pleasure. The disadvantage of the aneroid is that it is apt to vary from time to time, and requires to be compared once in two or three weeks, or even oftener, with a mercurial manometer to ascertain the true reading. It is, therefore, always necessary to have a mercurial manometer as well (Fig. 30).

Standardisation of Aneroids. — This can easily be done in less than two minutes by the arrangement shown in Fig. 30.

In the first edition of this book I described and figured a large number of instruments for

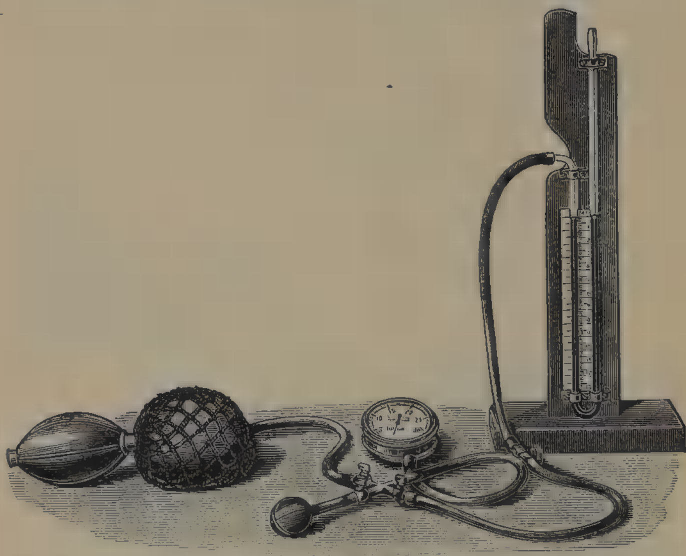


FIG. 30.—Author's apparatus for ascertaining the correctness or amount of error in an aneroid sphygmomanometer. By means of a three-way stopcock, both the aneroid and a mercurial manometer are put into communication with a pressure-bulb of a spray apparatus. The pressure is then raised 5 mm. at a time, and the readings of the mercurial and aneroid compared at each pressure show the amount of variation between them and the corrections necessary in the readings of the aneroid.

taking blood-pressure, but the measurement of blood-pressure has become so common now that it is almost unnecessary to mention more than one or two, as I have done. Other sphygmomanometers have also been described by Janeway in his *Clinical Study of Blood Pressure*.[12]

Method of using Sphygmomanometers.—In using a bulb apparatus, such as von Basch's or Potain's, the bulb is simply placed on the radial artery as it passes over the radius and compressed with the index finger, while the pulse nearer the hand is felt with the middle finger. The bulb is then pressed until the pulse ceases to be felt, and the pressure is read off on the index. Instead of using two fingers of the same hand it is better to compress the bulb with the finger of one hand and to feel the pulse with the finger of another, while the artery beyond can be compressed with a third finger. When the bulb consists of different thicknesses of india-rubber, the thicker part ought to be placed outside and the thinner part next the artery. The hand should be kept at the level of the heart.

Fallacies in using Bulb Instruments.—Unless the elastic bulb is placed over the end of the radius so that the arteries can be compressed between it and the bulb, and not over the soft tissues, too high a reading is obtained. If the palmar arch is dilated the recurrent pulse through it from the ulnar arteries may cause the pulse to be felt after the radial has been completely compressed by the bulb. To avoid this, the palpating finger should be placed on the radial artery with the tip pointing upwards. Any recurrent pulse is then stopped by the pulp of the finger, and the central radial pulse is felt by the finger-tip. Instead of this, two fingers may be used, as already mentioned.

Armlet Sphygmomanometers. — In using these, the armlet is fastened round the arm and

inflated by a small india-rubber hand-pump until the pressure is sufficiently great to stop the pulse. This point is noted, and the pressure is then increased a little further; air is then gradually let out, and the pressure is again noted when the pulse begins to reappear. In this way one has actually two observations made close together of the pressure which stops the flow of blood in the artery.

In a number of observations which I have made it has appeared to me that one sometimes gets a difference of 5 mm. between the values obtained when raising the pressure and that obtained with a falling pressure, the former being the higher.

Fallacies of the Armlet Sphygmomanometer.—The original armlet of Riva Rocci was too narrow and gave too high a reading, but with the armlets now commonly used not less than 12 centimetres or 5 inches broad, as recommended by von Recklinghausen,[13] the reading is generally correct.

There has been a good deal of discussion regarding the effect of rigidity of the arteries upon the values obtained by the armlet sphygmomanometer.[14] As a rule, the effect of somewhat rigid arteries is not very great, but whenever the vessels are felt to be rather rigid it is advisable to apply the instrument not to one arm only, but to both arms, or even to the forearm as well. The rigidity of the arteries, as a rule, does not affect all the vessels equally, and if different values are obtained the lowest should be selected.

Though the rigidity of stiff arteries does not as a rule greatly affect the values obtained by the sphygmomanometer, yet if the artery is in a state of contraction it opposes more resistance to compression, and the reading may therefore be too high.[15]

It has seemed to me that in very muscular or very fat limbs the reading of the band instrument is too high, and ought not to be accepted at once, but should be compared with readings obtained by a bulb instrument on the radial artery, which is simply covered by skin, so that the muscle cannot interfere. As a possible source of error this seems to me to have received little attention.

Systolic Pressure.—The pressure at which the pulse is obliterated by the sphygmomanometer indicates the systolic pressure or maximum height to which the tension within the artery is raised by the wave of blood driven into the aorta by the heart. In cases where the pulse is very irregular the highest pressure may only be noted with every third, fourth, or fifth beat, or even seldomer.

According to my own observations made in the sitting posture with a broad armlet, I find that from 8 to 14 years of age the maximum pressure is about 90 mm. From 15 to 20 years it is about 100 to 115 or 120 mm. From 21 to 65 years of age it is from 120 to 135 or 150 mm., the common pressure being 125 or 130 mm. Above 65 years, if the arteries are elastic, the pressure may still remain 135 to 150. If the arteries are rigid, it may go up to 180 or 200 mm.

or even higher. In women the pressure is as a rule 10 or 15 mm. lower than the corresponding pressure in men, and in strong athletic men it may be 15 mm. above the average. Though these values may not absolutely coincide with those of other observers, I think they are very nearly the truth.[16]

Some observations I have made on natives of India have yielded lower, and some on Canadians have yielded higher pressures than these.

Effect of Food on Blood-pressure.—Food usually raises the blood-pressure and quickens the pulse, but the effect depends much on its quantity, quality, and temperature. Much hot food or hot liquid put into the stomach will stimulate the heart, which rests on the stomach with only the diaphragm between, and thus tend to raise the pressure; but the warmer blood will cause the vessels to dilate, and the ultimate result as regards blood-pressure will depend on the preponderance of one or other of these factors. If they be nearly equal the pressure may remain unchanged though the pulse may be quicker.[17]

Effect of Exercise on Blood-pressure.—The effect of exercise differs according to its amount and duration, the time of day, and condition of the body. In exercise of any kind numerous muscles contract either simultaneously or successively. Each muscle as it contracts presses on the blood-vessels within it and drives the blood out with a spurt.[18] But during its contraction the arteries supplying it dilate,[19] and

thus the blood flows more freely through it, unless it presses so much on the arteries as to lessen or even stop the flow through them. But when the contraction ceases and the pressure on the arteries is thus removed, the blood pours through them.[20] If the exertion requires such

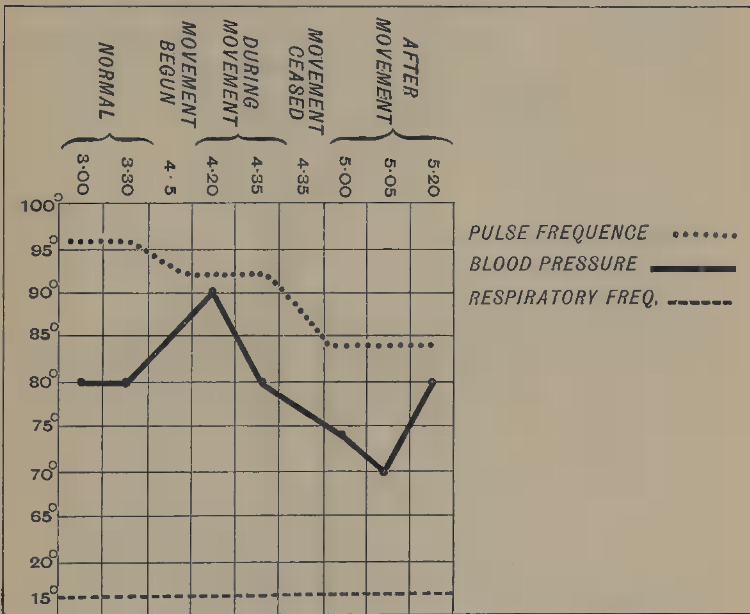


FIG. 31.—Effect of exercise on pulse and blood-pressure. (Brunton and Tunnicliffe.)

strong muscular contraction as to stop the flow through them during its continuance, it is obvious that the tension must almost of necessity rise considerably or even greatly, and this is what does occur.

Even moderate exercise tends to raise the tension at first. But as the arteries of the

muscles dilate, the tension falls even during the continuance of the exercise and continues to fall for some time afterwards. This is well shown in the accompanying curve, which represents the results obtained by Dr Tunnicliffe and myself in some experiments on this subject (Fig. 31).[21]

Potain found that the effect of exercise varied according to the time of day and condition of the person. When taken in the morning, fasting, it almost always lowered the tension; but when taken in the afternoon, three hours after a meal, it generally increased the tension.[22]

Effect of Emotion. — The effect of emotion may be very great. In 1903 I had arranged with Professor Kronecker to make some observations on the blood-pressure in workmen in the Jungfrau tunnel, where we were to meet each other. When I reached the station at Grindelwald I found the train quite full, so that all chance of meeting my friend, who was to come from Lauterbrunnen, seemed to be gone. I was greatly annoyed, but could do nothing to help it, and so I sat down and took my own blood-pressure. To my astonishment I found it had gone up from 120 mm., which was my normal, to 160 mm., the increase amounting to no less than one-third of my normal. I had only walked a few steps slowly before taking the pressure, so that there was nothing but the emotion to cause the rise.

Diastolic Pressure. — Diastolic pressure is the minimum to which the blood-pressure sinks during the interval between the cardiac beats, when no blood is coming into the aorta from

the heart, and the arterial system is emptying itself through the capillaries into the veins. It varies, therefore, with the length of that interval, and with the strength of the heart, the amount of blood sent into the aorta at each systole, and the patency of the capillaries. In a general way, just as the systolic pressure depends greatly on the strength of the heart, so the diastolic depends on the degree of contraction or relaxation of the capillaries.

Measurement of Diastolic Pressure. — An easy method of ascertaining the diastolic blood-pressure clinically is by auscultation. This appears to have been first used by Korotkow.[23] A stethoscope is placed, or a small phonendoscope is tied over the brachial artery below the armlet. When there is no pressure no cardiac sound is heard, but as the pressure is raised a "thud, thud" usually makes its appearance quite sharply. This continues until the maximum pressure is reached, when it stops abruptly. On again lowering the pressure, the "thud, thud" reappears and continues until a lower point is again reached when it ceases to be heard. The disappearance of the sounds at the higher level usually coincides very nearly with the systolic pressure as obtained by palpation of the radial artery. The appearance of the sounds at the lower level with the rising pressure, or their disappearance with a falling pressure, indicates the diastolic pressure. According to Oliver, the range of pressure over which the sounds are heard becomes shorter and the sounds feebler when the heart is weak.[24]

Another method of ascertaining the diastolic pressure is by observing the amount of oscillation that occurs in the walls of the artery at each pulse. Marey and Mosso found that this is at its maximum when the pressure inside and outside the artery is nearly equal.[25] By practice some people can distinguish by the finger alone when the radial pulse is largest, and thus ascertain the diastolic pressure. For this purpose the pulp of the last phalanx and not the finger-tip should be placed on the artery, and the observation repeated several times, raising and lowering the pressure in the armlet.

Instruments for ascertaining Diastolic Pressure.—Oscillations can be seen in an ordinary sphygmomanometer, mercurial or aneroid, but they can be observed more easily when they are more extensive. This is the case in Oliver's sphygmometers, both old and new, especially in the latter, which has a coloured fluid index working against a column of compressed air.[26] The scale is long, and the amount of oscillation is easily noted. The pressure can be alternately raised and lowered with great exactitude by means of a bag containing air, and placed in a kind of screw clamp.

In Sahli's sphygmobolometer the oscillations are shown in a similar way, but the actual pressure is shown by a second mercurial column which is also connected to the armlet, and is contracted at one point so as to prevent oscillations in it.[27]

Von Recklinghausen's[28] instrument is an

aneroid with a long index and large disc, so as to give amplitude to the oscillation. Pachon's[29] oscillometer consists of two aneroids, one within the other. The outer has a disc showing the pressure. When the inner is connected with the outer so that the pressure in both is alike, the long index which works on a large disc does not oscillate, but when the communication is stopped the index of the inner manometer makes large oscillations.

To measure the extent of oscillation exactly with any of these instruments is not always easy, but when the oscillations are recorded on paper as they are by Erlanger's,[30] Hirschfelder's,[31] or Gibson's[32] recording sphygmomanometer, the oscillations can be measured with compasses and their exact size determined.

Relation of Systolic to Diastolic Tension. Pulse-pressure.—The name pulse-pressure has been applied to the oscillation or difference between the systolic and diastolic tensions. Its use is to indicate the strength of the heart in relation to the resistance it has to overcome.

Strassburger[33] and Janeway[34] estimate the pulse-pressure as being ordinarily equal to one-fourth of the systolic pressure. But this relationship may vary considerably. When the pulse is slow there is more time for the blood to run out from the arteries into the veins in the interval between the beats of the heart, and so the oscillation of tension, or difference between the systolic and diastolic pressures, is greatly increased. On the other hand, when the pulse is quick there is little time

for the blood to flow out, and so the difference between the systolic and diastolic is small. In addition to this, when the pulse is slow there is more time for the heart to fill completely, and the amount expelled at each systole into the aorta is therefore greater, while it is smaller than normal when the pulse is accelerated. There is thus a twofold reason for the difference between the systolic and diastolic pressures with a slow and a quick pulse.[35]

This may be rendered clearer by the diagram (Fig. 32), where the dark line shows a trace which might be obtained by a manometer with

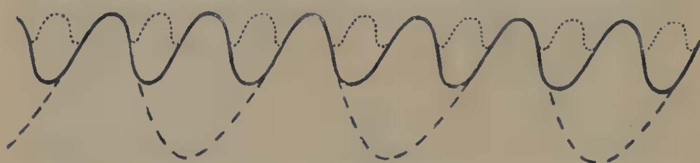


FIG. 32.—Diagram to show the effect of pulse-rate on oscillation of tension or pulse-pressure.

a moderately quick pulse. The interrupted line shows the large oscillations caused by a slow pulse, and the finely dotted line those caused by a rapid pulse. In these curves the power of the heart is supposed to remain the same. Under this condition a slow pulse causes great oscillation and a quick one small oscillation (Fig. 32).

But the power of the heart is a very important factor, and if strong in proportion to resistance it will cause large oscillation. If feeble, it will cause small oscillation.

Another important factor is the condition of the capillaries. If dilated, the blood flows quickly through them and oscillation is great. If

contracted, the flow is slow and the oscillation small (Fig. 33).

These points may be made clearer by using as an example some curves of blood-pressure which A. B. Meyer and I took in 1867 in du Bois-Reymond's laboratory in Berlin (Fig. 33).[36] The first section of the diagram shows the normal pressure, the second the pressure after digitalis had begun to exert its action, and the third

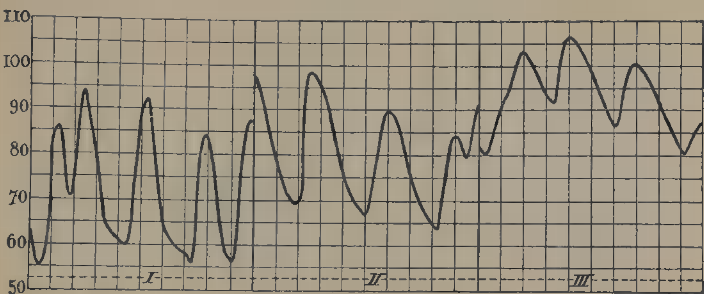


FIG. 33.—Tracing of the blood-pressure in a dog under the influence of digitalis. I, II, and III show progressive slowing of the pulse, rise of blood-pressure, and diminished oscillation due to contraction of the arterioles.

when the action of digitalis was well marked. The general effect of the drug is to slow the pulse, raise the tension, and increase the actual force of each beat of the heart.

The rise of tension is evidently due to contracted capillaries, for if they remained of the same size in the third section as in the first, the higher tension should drive the blood more quickly through them and the curve should fall more quickly during diastole, whereas the contrary is the case. The power of the heart is

increased because it drives the blood into the aorta against a higher arterial pressure, but it is not increased in proportion to the resistance.

Significance of Pulse-pressure or Oscillation.—This is perhaps most easily put in a tabular form.

	Tension.	Oscillation.	Heart.	Vessels.
1.	low	much	strong	dilated
2.	,,	little	weak	,, (probably)
3.	moderate	much	strong	moderately contracted
4.	,,	little	weak	,,
5.	high	much	strong	contracted
6.	,,	little	weak	,,

These conditions are represented diagrammatically in Fig. 34.

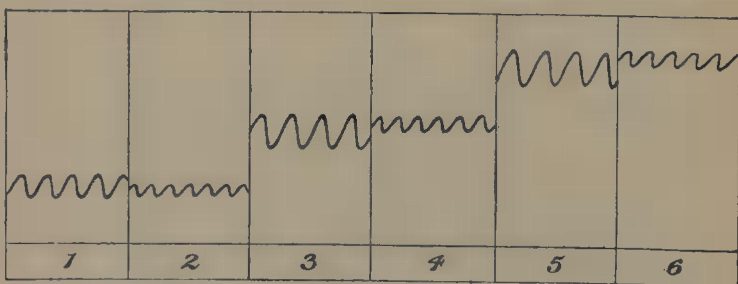


FIG. 34.—Diagram to represent the relation between arterial tension and pulse-pressure.

In 6 the actual power of the heart may be greater than normal, but it is less in proportion to the resistance it has to overcome.

Size of Vessels.—A most ingenious instrument for measuring the size of the arteries has

been devised by Dr Oliver, and is called by him the arteriometer.[37]

Measurement of Pressure in the Veins.—This may be done by choosing any convenient portion of a subcutaneous vein, and pressing a sphygmomanometer upon its distal end with sufficient force to stop the flow of blood. The proximal part is then emptied of blood by pressing the tip of a finger along it. The pressure of the pad or bulb is then relaxed, and the pressure noted at which the vein again fills.[38]

A simple way of roughly estimating the venous pressure is to notice at what height above the level of the heart the veins of the hand become empty. Normally, they should do so about the level of the third rib, or a little above. The greater the venous pressure, the higher must the hand be raised.

Measurement of Pressure in the Capillaries.—The method of doing this we owe to N. von Kries and Ludwig.[39] It consists in pressing down a piece of glass on the skin by a weight or spring, and noting the lowest pressure at which the skin becomes white. It is best done on the finger or lobe of the ear.

Another method is that of von Basch, who employs a thistle-funnel cut short, and having a side-tube in the thistle by which it can be connected through a T-tube with an aneroid and air-bulb. The top of the thistle is covered by a thin piece of glass; the lower end is fastened by cement on the patient's finger just above the nail. The pressure is then raised by compressing the air-bulb; the point is noted

when the skin under the end of the funnel becomes pale, and the pressure is read off on the aneroid.[40] This method can be applied also to ascertain the pressure in veins.

LITERATURE.

[1] von Basch, *Verhandl. d. Physiol. Gesellsch. zu Berlin*, Jahrg. 1879-80, No. 7; *Berl. klin. Wochenschr.*, 1887, Nos. 11-16. For description of experiment, *vide* also Lauder Brunton, *Lancet*, 17th October 1908, p. 1126.

[2] von Basch, "Der Sphygmomanometer u. seine Ververtung in der Praxis," *Berl. klin. Wochenschr.*, 1887, vol. xxiv., p. 181.

[3] Potain, *La pression arterielle de l'homme*, etc. (Paris: Masson, 1902); and *Arch. de Physiol.*, 1889, vol. i., p. 556, and 1890, vol. ii., p. 300.

[4] Oliver, *Blood and Blood Pressure* (London: Lewis, 1901), p. 114; *Quart. Journ. of Exp. Physiol.*, vol. iv., No. 1, p. 45.

[5] Hill, *Further Advances in Physiology*, p. 122 (London: Arnold, 1909).

[6] Sahli, *Lehrb. d. Klin. Untersuchungsmethoden*, Bd. i., 6 Aufl., 1912; and "Sphygmobolometrie," *Corr.-Bl. f. schweiz. Aerzte*, 1911, No. 16; *Deutsch. med. Wochenschr.*, 1907; *ibid.*, 1910, No. 47; *Ztschr. f. klin. Med.*, vol. 72, Nos. 1 and 2.

[7] Gaertner, *Wien. med. Wochenschr.*, 1899, vol. xlix., p. 1412.

[8] Riva Rocci, *Gaz. Med. d. Torino*, 1896, vol. xlvii., p. 981.

[9] Hill and Barnard, *Brit. Med. Journ.*, 1897, vol. ii., p. 904

[10] Hawksley, *vide* C. J. Martin, *Brit. Med. Journ.*, 22nd April 1905, p. 865.

[11] Lauder Brunton, *Lancet*, 17th October 1908, p. 1126.

[12] Janeway, *Clinical Study of Blood Pressure* (New York and London: Appleton, 1904).

13 von Recklinghausen, *Arch. f. exp. Path. u. Pharm.*, 1901, vol. xlvi., p. 78; and *ibid.*, 1906, vol. lv., pp. 375 and 412; C. J. Martin, *Brit. Med. Journ.*, 22nd April 1905, vol. i., p. 865.

14 William Russell, *Arterial Hypertonus*, etc., p. 72 (Edinburgh and London: Wm. Green & Sons, 1907); Herrington and Womack, *Proc. Roy. Soc. of Med.*, London, 1909, vol. ii., p. 37.

15 *Vide* Kronecker and Magnus Schmidt, *Arch. f. Anat. u. Physiol.*, *physiol. Abt.*, 1909, p. 331.

16 Janeway, *op. cit.*, p. 108 *et seq.*

17 Janeway, *op. cit.*, p. 117; Cabot and Bruce, *Amer. Journ. Med. Sci.*, 1907, vol. cxxxiv., p. 491; Potain, *Pression arterielle*, etc., p. 53 (Paris: Masson, 1902).

18 Ludwig and Sadler, *Ludwig's Arbeiten* for 1869 (Leipzig: Hirzel, 1870), p. 89.

19 *Ibid.*, p. 96.

20 *Ibid.*, p. 90.

21 Lauder Brunton and Tunnicliffe, *Brit. Med. Journ.*, 16th October 1897, vol. ii., p. 1073.

22 Potain, *Pression arterielle*, etc., p. 60 (Paris, 1902).

23 Korotkow and Janowski, quoted by Fellner, *Verhandl. d Kongress f. inn. Med.*, Wiesbaden, 1907, vol. xxiv., p. 404 *et seq.*; Oliver, *Proc. Roy. Soc. of Med.* London, 28th June 1910, vol. iii., pt. ii., Med. Sect, p. 207.

24 Oliver, *Quart. Journ. of Exp. Physiol.*, 1911, vol. iv., p. 44.

25 Marey, *Trav. Lab.*, 1876, vol. ii., p. 313, and 1878 vol. iv., p. 126; Mosso, 1895, *Arch. Nat. de Biol.*, vol. xxiii., p. 177; Roy and Adami, *Practitioner*, 1890, vol. xlv., p. 32.

26 Oliver, *Quart. Journ. of Exp. Physiol.*, 1911, vol. iv., p. 50; Eckenstein, *Brit. Med. Journ.*, 1910, vol. ii., p. 1765.

27 Sahli, *Corr.-Bl. f. schweiz. Aerzte*, 1911, No. 16.

28 von Recklinghausen, *Arch. f. exp. Path. u. Pharm.*, 1906, vol. lv., p. 432.

29 Pachon, *Compt. rend. de la Soc. de Biol.*, 8th and 15th May 1909, vol. lxvi., pp. 723 and 726.

30 Erlanger, *Amer. Journ. of Physiol.*, 1902, vol. vi., p. 22; 1904, vol. xi., p. 14.

[31] Hirschfelder, *Diseases of the Heart and Aorta*, p. 21 (Lippincott Co., 1910).
[32] Gibson, *Proc. Roy. Soc.*, Edinburgh, 1907-8, vol. xxviii., p. 343 *et seq*.
[33] Strassburger, *Ztschr. f. klin. Med.*, vol. liv., p. 377.
[34] Janeway, *Clinical Study of Blood Pressure*, p. 109 (New York and London, 1904).
[35] Lauder Brunton, *Brit. Med. Journ.*, 5th November 1910, vol. ii., p. 1389.
[36] Lauder Brunton and A. B. Meyer, *Journ. of Anat. and Physiol.*, 1873, vol. vii., p. 134.
[37] G. Oliver, *Blood and Blood Pressure*, p. 127 (London : Lewis, 1901).
[38] G. Oliver, "Lecture on Hamomanometry," *Lancet*, 22nd July 1905, vol. ii., p. 201.
[39] Ludwig and Kries, *Ludwig's Arbeiten*, 1875, p. 69.
[40] v. Basch, *S. Arch. des scienc. biol. d. St Petersb.*, 1904, vol. xi., suppl., pp. 117-136.

CHAPTER VI

EXAMINATION OF THE CIRCULATION

Cardiographs — Apex - beat Cardiograms — Sphygmographs — Carotid Pulse — Mode of Applying the Sphygmograph — Sphygmograms — Fallacies — Inverted Tracings—Venous Pulse—Pseudo-pulsations in Jugular Vein—Sphygmographic tracing of Venous Pulse—Characters of the Venous Pulse—Propagation of the Pulse-wave — Delay — Practical Use of the Sphygmograph—X-ray Examination of the Heart—Skiagrams—String Galvanometer—Leads—Electrocardiograms—Coagulometer—Viscosity of the Blood.

Cardiographs.—All the instruments I have hitherto described have been chiefly for measuring the amount of blood-pressure, or the size of the artery, but they do not give us any indication of the mode of contraction of the heart or the nature of the pulse-wave. These have chiefly been worked out by instruments devised by the late Professor Marey,[1] and the principle upon which most of them depend is that of the transmission of motion by air from one elastic vessel to a second, on which rests a light lever which amplifies the movements and records them on a revolving cylinder. By introducing an elongated bulb through the aortic valves into the

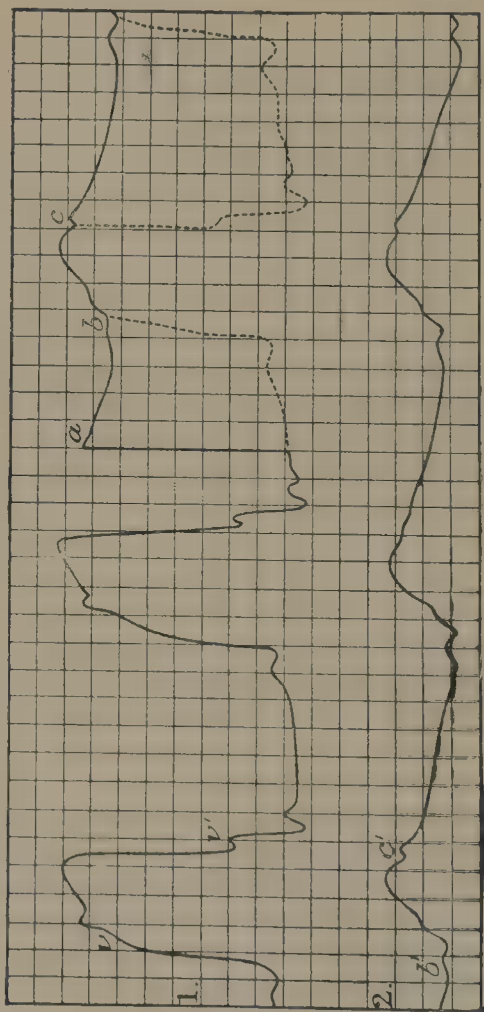


FIG. 35.—Tracings of the ventricular systole (1), and of the aortic pulse (2). The parts *b c* and *b′ c′* are common both to the ventricular and aortic tracing. At this point the aortic valves are open, and the ventricle and aorta are in free communication; *b′*, in the second tracing, marks the point where the blood begins to flow into the aorta; *v* marks the point where the mitral valves, and *v′* where the sigmoid valves, close. (After Marey.)

ventricle, Marey obtained tracings of the changes in pressure throughout the ventricular cycle, as shown in Fig. 35, where the upper tracing shows the rise of pressure in the heart, and the lower in the aorta. In the cardiac tracing there is first a slight rise, due to the auricular contraction, then a sudden rise, which becomes somewhat slower as it increases. At the top of this is a plateau showing several oscillations, then a sudden descent, marked at its end by a little wave, and then an almost level line, after which the same sequence again occurs.[2] The alteration in rapidity of ascent, which takes place about the middle of the systole, probably indicates the time at which the auriculo-ventricular valves become screwed together, for this is the kind of closure actually witnessed (p. 74), and the aortic valves are forced open by the increasing pressure behind. The oscillations which occur on the plateau, according to Marey, do not indicate mere vibrations of the auriculo-ventricular valves, but real oscillations in them and in the blood on both sides of them. The sharp fall indicates the diastolic relaxation of the ventricle, and the little wave at the end marks the time of closure of the sigmoid valves.

When the bulb is withdrawn from the ventricle into the aorta, a tracing is obtained which is almost exactly like that of the ventricle with the lower part of it cut off, and a gradual descent substituted for the sudden fall. If the aorta were rigid, this form of curve would be transmitted on to the periphery, and we do,

indeed, find that the radial pulse-tracing shows the characters of the aortic pulse, namely, the flattened plateau and slow, rather even, descent whenever the elasticity of the arteries is impaired by atheromatous change, as in old people, or by great distension from high arterial pressure, as in cases of Bright's disease (Fig. 36).[3]

Apex-beat Cardiograms.—The cardiograph which is used to register the apex impulse is a tambour with a spring to press it against the

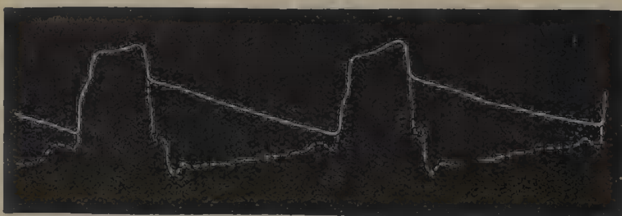


FIG. 36.—Diagram to show the analogy of the senile pulse to the ventricular beat. (After Marey.) The unbroken line is the sphygmographic tracing; the dotted line shows the ventricular tracing.

chest wall, and this is connected by india-rubber tubing with a writing tambour and lever. The tracing is somewhat like that of the aorta, but it is higher and falls more abruptly. The abruptness of the fall depends to a considerable extent on the pressure of the cardiograph.[4] The tracing may vary very much in the same individual under various conditions.[5]

Sphygmographs are instruments for magnifying and recording the movements of the pulse. In most of them a spring rests upon the artery and its movements are transmitted to a

lever, which greatly magnifies them and records them upon a moving surface either directly or through a tambour. There are many forms. Of these, Marey's [6] original one probably gives the most accurate records; but, on account of its cheapness, portability, and ready application, Dudgeon's [7] is the most favoured in this country. Jacquet's is similar in form,[8] but is provided with a time-marker and also a tambour for registering at the same time the movements of the apex beat and respiration. Mackenzie's polygraph can also register these latter movements, and in it the movements of the pulse both in the radial artery and jugular veins, are transmitted to a tambour.

One exception to the rule I have just given is Kronecker's sphygmograph, which gives the true form of the pulse without the tracing being deformed in any way by the oscillations of the instrument. It consists of a modified capillary electrometer, and the movements of a very fine mercurial column are photographed on a revolving cylinder.[9] One interesting point which this brings out is that the pointed top of the ascending curve is not altogether due to a jerk of the recording lever, as is generally assumed, but really indicates the abrupt shock given to the artery by the impact of blood driven into it by the ventricular systole.

Carotid Pulse.—For this artery it is most convenient to use a tambour with a knob and spring like a small cardiograph, rather than a lever. The pulsations are transmitted to a writing tambour.

Application of the Sphygmograph. — The radial artery is the most convenient, and the tracings are most accurate when taken from it just as it lies over the radius. Sometimes such tracings show very small amplitude and better ones are got from the artery a little higher up. The pelotte of the sphygmograph ought to be exactly over the artery, and to ensure this it is well to mark the vessel with a blue dermatograph pencil before tying on the instrument. It is usually fastened on by straps, but a great saving of time is effected by using two elastic bands, which are simply twined together behind the wrist without tying them. They generally hold tightly enough, and are easily unfastened as well as fastened. When the elastic is becoming worn it must be replaced by new. In most patients it is advisable to extend the wrist somewhat, which can be done by placing a book or pad of some kind under it.

It is sometimes difficult to get the lever to write exactly on the right part of the paper, and to overcome this difficulty I have had a screw adjustment applied by Mr Hawksley to Dudgeon's sphygmograph.

Sphygmograms. — In a perfectly healthy person the arteries are circular in section. They dilate as each wave of blood is sent in from the heart, and they contract during the intervals of the cardiac pulsations; but this dilatation and contraction is very slight and is not the pulse which is usually felt by the finger. In feeling the pulse the artery is squeezed out of shape by the pressure of the finger, so that

the section becomes oval instead of circular. The increased pressure within the vessels at each beat of the heart tends to restore the circular section, and it is this movement which is felt by the finger and recorded by the sphygmograph. The pulse wave as thus recorded by the sphygmograph in the radial artery differs a good deal from that in the carotid. In the carotid the systolic rise is much like that which occurs at the end of the ventricular contraction, Fig. 35, but it is much modified by the elasticity of the arteries on its

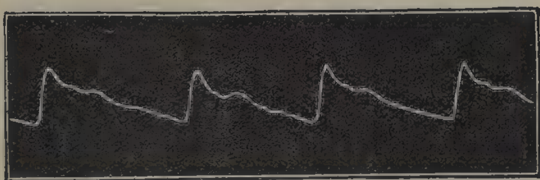


FIG. 37.—Tracing from normal pulse.

way to the radial, so that in a normal sphygmogram we notice a fairly sudden and extensive systolic rise followed by a moderately quick fall for a certain distance, then a second rise followed by a second slower fall (Fig. 37).

A quick rise indicates that the heart is acting strongly relatively to the resistance opposed to it by the pressure of blood in the arteries. It may be due either to a strongly acting heart or low arterial pressure from emptiness of the arteries.

A slow rise indicates that the heart is relatively feeble. It may be due to actual weakness

of the ventricle or to the great resistance opposed to it by high blood-pressure.

A quick fall indicates that the arterial system empties itself easily either through the systemic capillaries into the veins or backwards into the heart, or both. In aortic regurgitation during the diastole the blood flows back into the heart as well as onwards through the capillaries. The arterial system therefore becomes abnormally empty and the pulse tracing falls very low. At the same time the ventricle gets

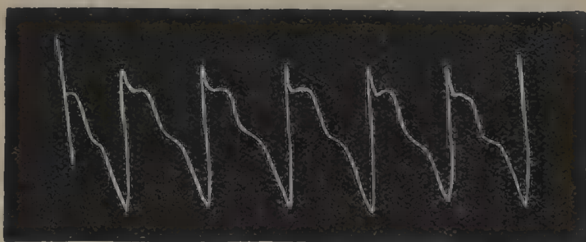


FIG. 38.—Tracing from a case of aortic regurgitation, showing hook at top of tracing, sudden fall, and extensive movement.

a double supply of blood, onward from the auricle and backward from the aorta. It therefore shoots a large wave into the aorta, so that the pressure rises suddenly and greatly. This causes the lever to ascend so quickly that its own inertia carries it too far and a little crochet or hook is formed at the summit of the tracing (Fig. 38).

When the quick fall of the sphygmographic tracing is due to dilated capillaries it is usually

broken by a second wave, known as the dichrotic wave (Fig. 39). This is usually all the more marked the lower the tension is. When the tension is raised it may disappear completely, and when the tension is very low it may become so marked as almost to rival the primary wave in height. It is then called hyperdichrotic. The most marked tracing of it that I ever obtained was from a youth who had had very profuse hæmoptysis, so that he had become almost drained of blood.

As a rule, exaggeration of the dichrotic wave

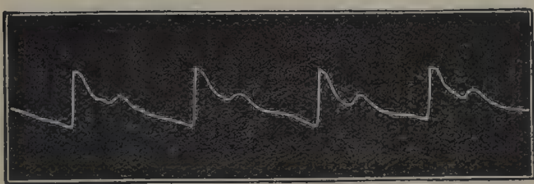


FIG. 39.—Dichrotic pulse.

means increased power of the heart in relation to the resistance it has to overcome, so that the elasticity of the arteries is fully called into play, just as an elastic ball thrown against the floor rebounds higher the more force that is used. When the aortic valves are incompetent, this rebound is less marked or absent. This is one of the arguments used to prove that the dichrotic wave is due to a rebound from the aortic valves rather than from the periphery. Sometimes the descending limb is broken by three or even four waves forming a trichrotic or tetrachrotic pulse. These are supposed to be due to waves

from the aorta reflected back from the peripheral vessels and then back again.

A slow fall indicates that the blood is flowing slowly through the capillaries. It may occur in perfectly healthy persons from contraction of the capillaries by cold (1, Fig. 40),[10] and is generally present in elderly people with high tension.

Fallacies in Sphygmograms.—Quite apart from any imperfections in the instrument

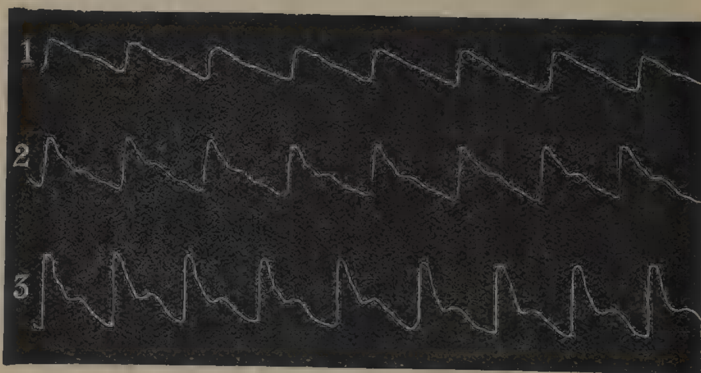


FIG. 40.—Effect of cold in contracting the capillaries and raising the blood-pressure, and of warmth in dilating the capillaries and lowering the blood-pressure. 1. Effect of cold. 2. Normal. 3. Effect of warmth. (After Marey.)

employed, the way in which the sphygmograph is applied to the arm may cause very different tracings to be obtained. If the pelotte does not rest fairly on the artery the pulse wave may appear very small and a dichrotic wave may disappear (Fig. 41).

In old persons with somewhat thickened arteries the senile pulse with a marked plateau (p. 126) is common, but sometimes this character

is obscured (Fig. 42) and quite a different tracing is obtained (Fig. 43), because instead of the lever of the sphygmograph being simply raised at each

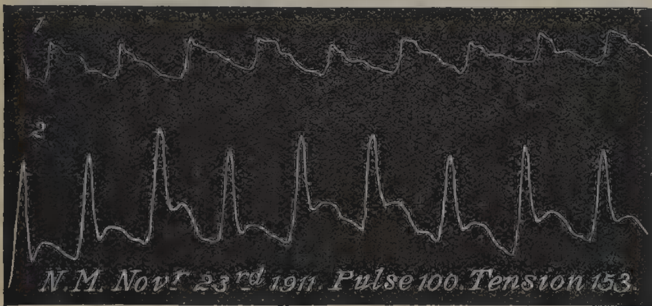


FIG. 41.—Different tracings produced by different applications of Dudgeon's sphygmograph in a case of pneumonia. The sphygmograph was not removed from the arm, but its position and pressure were altered between the tracings. The age of the patient was 72.

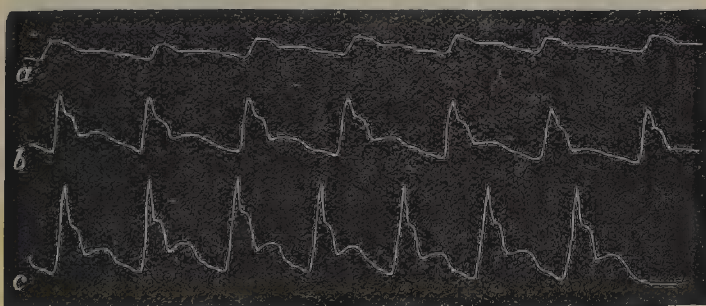


FIG. 42.—Three successive tracings from a pulse, taken at the same time and under the same conditions, but with altered application of Dudgeon's sphygmograph.

pulse by the increased tension in the artery, it is suddenly driven up by the longitudinal elongation, which is often distinctly visible in such cases.

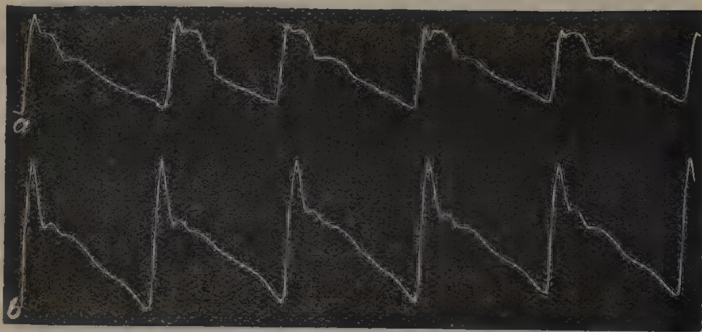


FIG. 43.—Two tracings from the same pulse. In *a* the senile plateau is distinct, in *b* it is masked by the sudden impulse given to the lever.

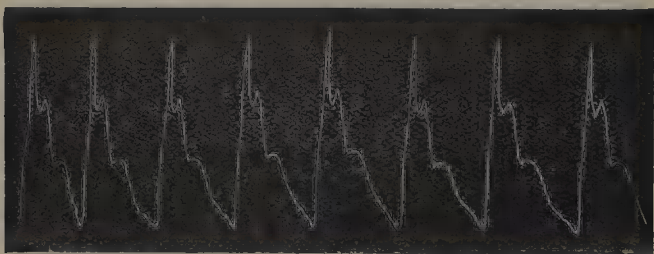


FIG. 44.—Tracing from a locomotive artery in a man aged 82.

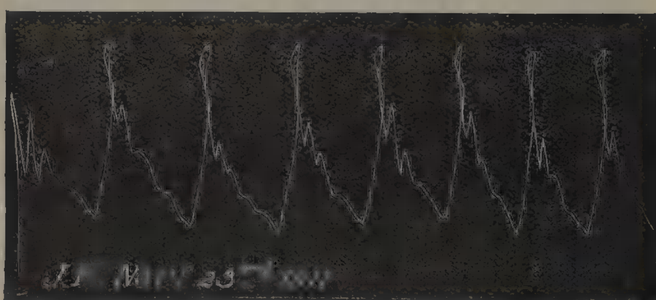


FIG. 45.—Tracing showing excessive and irregular movement of lever due to locomotive arteries. Patient aged 61; pulse 76, tension 235 mm.

In Dudgeon's sphygmograph the connection between the lever and pulse-pad is loose, and an obviously incorrect tracing is sometimes obtained (Fig. 45).

I have never obtained such inaccurate tracings with Marey's sphygmograph, and I regard it as a much more trustworthy instrument than Dudgeon's, but the ease and rapidity with which the latter can be applied render it much more convenient.

Inverted Tracings.—When the pelotte is placed at one side of a locomotive artery

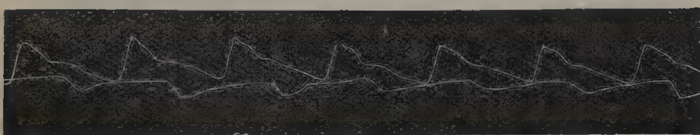


FIG. 46.—Inverted tracing. The upper tracing is the normal one, the lower is inverted. In taking these tracings the sphygmograph remained on the arm, but its position over the artery was slightly altered.

instead of upon it, the elongation of the artery gives a drag instead of a push to the pelotte, and an inverted tracing is produced (Fig. 46).

Venous Pulse.—As a rule, no pulsation is visible in any vein, but in tricuspid regurgitation the blood is driven back by the right ventricle through the auricle into the jugular vein, giving rise to visible pulsation.

Pseudo-pulsation in the left Jugular Vein.—In some persons an apparently well-marked pulsation occurs in the left jugular vein only. This is probably due to alternate compression and relaxation of the innominate vein by the pulsa-

tions of the aortic arch.[11] It can be imitated in the jugular of either side by alternately compressing it with the finger and releasing it.

Sphygmographic Tracings of Venous Pulsation.—The method of taking tracings from the jugular vein was introduced by Mackenzie, and it has added much to our knowledge of the physiology and pathology of the heart's movements.[12] The tracing is taken by a tambour and lever in the same way as a cardiogram, but in place of a cardiograph such as is used for the heart a small funnel or, better, a shallow metal pan is used as a receiver. One part of its circumference is flattened so as to allow it to be applied more closely above the clavicle. In using it the patient should lie on his back with his head and neck supported by a pillow, his head turned to one side and his neck flexed. The receiver is then pressed down on the jugular bulb, and the pulsations of the vein are transmitted to the tambour. If any difficulty is experienced in obtaining a tracing here the receiver should be moved a little more to the right and placed over the junction of the jugular and subclavian veins.

Characters of the Venous Pulse.—The tracing usually presents two rises and two falls in a cycle (Fig. 47). The first rise is large and sharp. It is due to the auricular contraction. The first fall is rapid, owing to the auricle having been emptied. The second rise is slow, and is due to the gradual filling of the auricle. The second fall is slight, and is due to the blood flowing into the empty ventricle. As the first sharp rise

coincides with the auricular systole, it allows the time of this to be exactly noted and compared with the carotid pulse, which nearly coincides with the ventricular systole. It is thus easy to ascertain whether the normal sequence between auricular and ventricular systoles exists, or whether any heart-block is present.

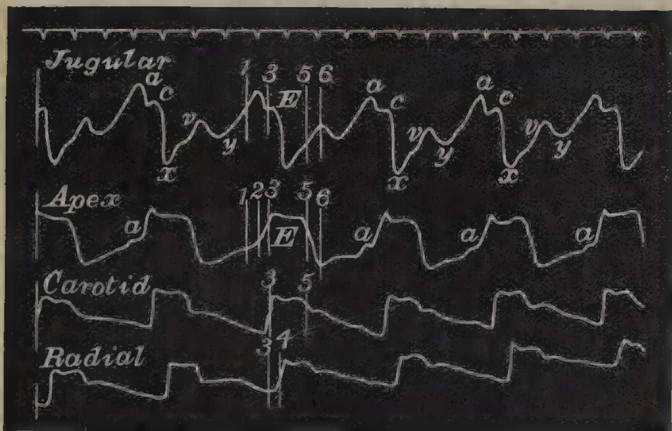


FIG. 47.—Venous pulse in the jugular and its time-relations to the apex beat and carotid and radial pulses. The perpendicular lines show the time of (1) Beginning of auricular systole; (2) beginning of ventricular systole; (3) beginning of carotid pulse; (4) beginning of radial pulse; (5) closure of semi-lunar valves; (6) opening of tricuspid valves. (After Mackenzie.)—From *Diseases of the Heart*, by James Mackenzie, M.D., F.R.C.P., p. 107. London: Froude, and Hodder & Stoughton, 1908.

For a method of showing diagrammatically the relative position of the curves and the delay in transmission, *vide* p. 418, Fig. 111.

Propagation of the Pulse-wave. Delay.—The pulse-wave travels at a rate of about 30 feet per second.[13] Counting from the commence-

ment of the opening of the valves, which takes about one-twentieth of a second, the pulse-wave takes one-tenth of a second to reach the carotid, and rather less than two-tenths to reach the radial artery. In timing cardiac murmurs it is, therefore, better to take the carotid than the radial pulse.[14]

Practical Use of the Sphygmograph.—The chief uses of the sphygmographic tracing are :—

(1) To show the presence or absence of elasticity within the arteries, as evidenced by the more or less complete modification of the systolic plateau.

(2) The strength or weakness of the heart, as compared with the pressure it has to overcome, as shown by the quick or slow rise during systole.

(3) The condition of contraction or relaxation of the arterioles, shown by the slowness or rapidity of the diastolic fall and by the more or less marked dichrotism.

It cannot replace the sphygmomanometer, but when used along with it may afford useful information regarding the condition both of the heart and vessels.

X-ray Examination of the Heart. — By placing a luminous vacuum tube at one side of the body, and a fluorescent screen upon the other,[15] the shadow of the heart is thrown upon the screen so that the size and movements of its different parts may be seen, hypertrophy, dilatation, or aneurism observed, and even heart-block diagnosed.

Skiagrams.—A sensitised plate may be put

in the place of the screen, and thus a permanent record of the condition of the heart is obtained.

String Galvanometer. — The detection of auricular fibrillation in man has only recently been rendered possible by the use of electrocardiograms. In 1876 Marey,[16] and in 1880 Burdon-Sanderson and Page[17] examined the electric changes which accompany the cardiac movements by means of a capillary electrometer, and in 1887 Waller[18] found with the same instrument that these electric changes can be observed in an intact animal. The introduction of the very delicate string galvanometer of Einthoven[19] has greatly increased the accuracy of observations.*

This instrument as described by Kraus and Nicolai consists of a very delicate quartz fibre, silvered to make it conduct, and stretched between the poles of a powerful electromagnet. When a current passes through the fibre it is deflected at right angles to the magnetic field. The ends of the wire are connected to two small pails containing saline solution. Into these the two hands, or one hand and one foot, of the patient are placed. The current produced by the heart is conducted from them through the wire, and according to the direction in which it passes the wire is attracted by one or other pole. The shadow of the wire is thrown by a

* The instrument and its employment and uses have been fully described by F. Kraus and Nicolai (*Das Elektro Kardiogramm*, Veit, Leipzig, 1910), and Lewis (*Mechanism of the Heart Beat*, Shaw & Sons, London, 1911).

strong light or reflected from the string on a revolving cylinder covered with sensitised paper. Before reaching the paper it passes through a small slit at right angles to the wire, so that only the motions of a point in the wire are recorded. If the wire cuts off the light from the paper its motions are indicated by a white line, but if the movement is recorded by reflection, the movements of the wire are in black. The fibre is so thin that it could not bear the strain of being stretched horizontally, so that in practice it is vertical, and the recording cylinder is horizontal; but as the curves are always read vertically, it is easier to understand their production when the apparatus is represented as in the diagram, in which position it would produce vertical curves (Fig. 48). The instrument used by Waller differs from this.

Leads.—Waller gives the subjoined system of leads:—*

Lead I.	Right hand and left hand	=	**Transverse.**
Lead II.	Right hand and left foot	=	Axial (=IV.).
Lead III.	Left hand and left foot	=	**Left lateral** (=V.).
Lead IV.	Right hand and right foot	=	**Right lateral** (=II., axial).
Lead V.	Left hand and right foot	=	Equatorial (=III.).
Lead VI.	Right foot and left foot	=	Inferior.
Lead VII.	Mouth and left hand	=	Left superior.
Lead VIII.	Mouth and right hand	=	Right superior.
Lead IX.	Mouth and left foot	=	Left inferior.
Lead X.	Mouth and right foot	=	Right inferior.

He regards the two feet as iso-electric, and consequently Lead III. (left lateral) and V. (equatorial) as practically equivalent; Lead II. (axial) and Lead IV. are also equivalent.

* *Lancet*, 24th May 1913, vol. i., p. 1435.

Setting aside the superior leads, the Leads I., IV., and III. are equal to Einthoven's * trio—viz., transverse, axial, and left lateral.

Electro-cardiograms.[20] — The electric condition of the base or apex of the heart is conducted to the arm or leg nearest it, and is thence transmitted to the galvanometer. The right arm or leg being nearest to the base shows its electrical condition, and the left arm or leg shows that of the apex. The best electro-cardiograms are got from the right hand and left foot, but it is more convenient to take them from the two hands.

The physiological fact on which they depend is that the excited part of a muscle becomes electro-negative (usually indicated by —) to the non-excited parts, which are therefore positive (+) to it.

If an excitation starts at one end, A, of a straight muscle with parallel fibres and travels to the other end, B, the electric variation would be that A would first be negative and then positive to B. This is known as diphasic variation. If equal currents were to start from both ends at the same time, but in opposite directions, they would neutralise each other, and there would be no deflection of the wire at all.

In a normal cardiogram there are three deflections or groups of deflection. The first is associated with the auricular, and the second

* Einthoven: "Ueber die Form des Menschlichen Electrocardiogramms," *Pflüger's Archiv*, vol. lx., p. 101, 1895; "Weiteres über das Electrocardiogramm," *Pflüger's Archiv*, vol. cxxii., p. 517, 1908.

and third with the ventricular, systole. These have been indicated by different letters by

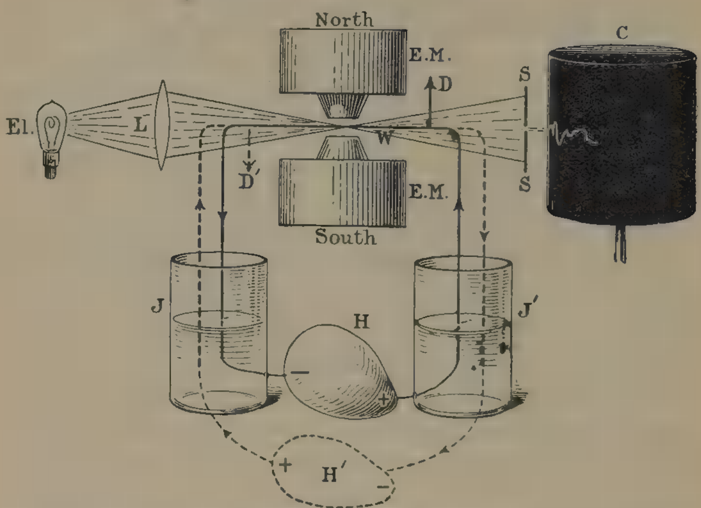


FIG. 48.—String galvanometer. (Very diagrammatic, so much so that it may be regarded by some as incorrect.)

E.M. indicates the poles north and south of a powerful electro-magnet, between which a metal string (wire), W, passes. Its two ends are placed in two jars containing saline solution, J and J′. Into J the right hand, and into J′ the left hand or left foot are placed, so as to conduct the current from the heart through the wire. H is the heart at the beginning of systole. The base is then negative, −, to the apex, +, and the current passes from it through the limbs and wire in the direction shown by the unbroken line. D indicates the direction in which the wire then moves. H′ is the heart at the end of systole, and the apex is then negative, −, to the base, +, so that the current passes in the opposite direction, as shown by the broken line, and the wire moves in the direction indicated by D′. El. is the source of light, and L the lens by which the light is concentrated on W, so as to throw its shadow on the recording cylinder C. S is a screen with a narrow slit in it to cut off superfluous light, and make the shadow of W sharper on the screen. As it is the *shadow* of the wire which is photographed on the sensitised paper on the cylinder, the curve appears white on a dark ground, unless the original curve is used as a negative from which to print copies. In practice also the wire is vertical, in order to avoid dragging, and the cylinder is horizontal.

various writers. The simplest is that of Waller, but a good one also is that of Nicolai,[21] who

indicates the auricular variation by *A* and the initial end of the ventricular variation by *I* and its final one by *F*. All three are succeeded (post) by slight variations in an opposite direction, which are indicated by *Ap*, *Ip*, and *Fp*. The variations *I* and *P* have slight opposite variations anterior to them, indicated as *Ia* and *Fa*. The

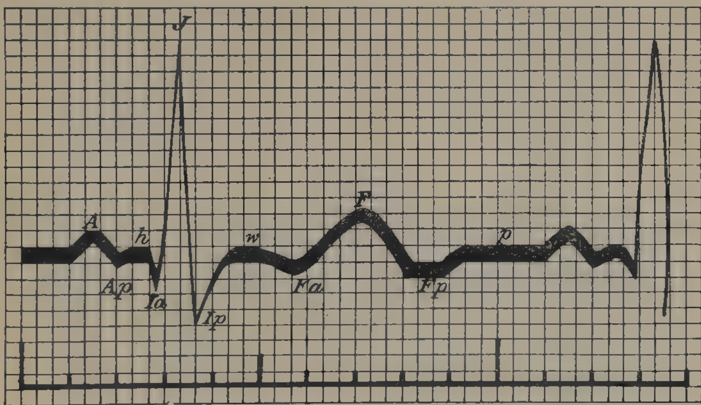


Fig. 49.—Diagram of an electro-cardiogram. (After Kraus and Nicolai.) *A* = auricular variation; *I* = initial variation; *F* = final variation; *Ap* = post-auricular negative variation; *Ip* = post-initial negative variation; *Fp* = post-final negative variation; *Ia* = ante-initial negative variation; *Fa* = ante-final negative variation: *h* = time lost in the bundle of His; *w* = time lost in the cardiac walls; *p* = pause of heart.*

* In Kraus and Nicolai's diagram, *w* (wall) is indicated by *t* (Treibwerk).

period when the excitation is passing through His's bundle is indicated by *h*; that time when it is passing in more or less different directions through the wall of the ventricle, so that they counteract one another, and no variation is observed, is indicated by *w*, and the pause in which there are no currents by *p*.

Different authors have denoted various deflections in an electro-cardiogram by different letters so that it is sometimes difficult to compare them As Waller was the first to discover the electro-cardiogram his nomenclature ought perhaps to be followed, and is certainly the simplest, but he does not give a letter of indication for all parts of the cardiogram, and I therefore append here a table of the letters used by different authors to designate the parts.

	Kraus and Nicolai.	Einthoven.	Waller.
Positive waves—			
Auricular waves	*A*	*P*	*A*
Ventricular waves initial	*I* or *J*	*R*	*V′*
Ventricular waves final	*F*	*T*	*V″*
Negative waves—			
After auricular	*Ap*		
After ventricular post-initial	*Ip* or *Jp*	*S*	
After ventricular post-final	*Fp*		
B fore ventricular initial	*Ia* or *Ja*	*Q*	
Before ventricular final	*Fa*		
Time of passage in His's bundle	*h*		
Time of passage in heart wall	*t* or *w*		
Pause of Heart	*p*		

This diagram is copied from Kraus and Nicolai's *Das Elektro Kardiogramm*, p. 201, but *I*, the first letter of "initial," has been substituted for *J*, and *w*, the first letter of "wall of heart," for *t*, the first letter of "Treibwerk."

By means of this instrument it is possible to settle many questions regarding the heart. By its means the occurrence of fibrillation of the auricles has been demonstrated, and Fig. 50

shows that stimulation of the vagi lengthens the time required for a stimulus to pass from the auricle to the ventricle[22]

Coagulability of the Blood.—Stoppage of the circulation through an artery by coagulation of the blood within it gives rise to the same symptoms as arrest of the circulation from any other cause, and when it occurs in one of the vessels of the brain it is sometimes exceedingly difficult to diagnose between bursting of a vessel

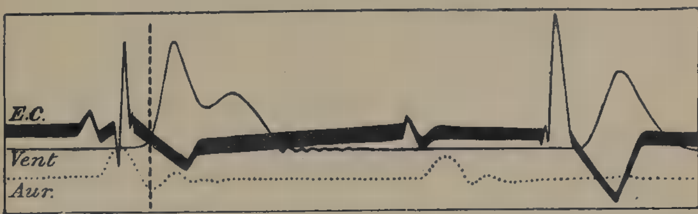


FIG. 50.—Electro-cardiogram during irritation of the vagus. *E.C.* is the electro-cardiogram. *Vent.* is a tracing taken mechanically from the ventricle, and *Aur.* one from the auricles. The upright dotted line shows the moment at which the stimulus is applied to the vagus. The time which elapses between the auricular variation and beat and those of the ventricle is exceedingly short before stimulation, and very long during it. (After Kraus and Nicolai.)

and consequent hæmorrhage and thrombosis. One of the important diagnostic points is, of course, arterial tension, because with a high arterial tension, hemiplegia, monoplegia, or aphasia are probably due to hæmorrhage; while if the tension is low, they are probably due to thrombosis. An additional means of diagnosis is the rapidity with which the blood coagulates. A good method of ascertaining this is Wright's.[23] It consists of a series of fine tubes into which the blood is drawn from a puncture in the finger. They are then placed in water

about the temperature of the body. At varying intervals one blows down the tube and the time is noted when the blood can no longer be blown out. This indicates the time of coagulation, and the interval between this and the filling of the tube is the coagulation time. It varies under different circumstances, a fairly average time being four minutes.[24]

Viscosity of the Blood. — It has already been mentioned (p. 16) that the arterial pressure depends upon the difference in quantity between the amount of blood forced into the aorta by the heart and the amount of blood which runs out into the veins through the arterioles and capillaries in the same time. The amount of blood which thus flows out from the arterial system depends:

1. Upon the amount of pressure in the aorta;
2. On the size of the efferent arterioles and capillaries; and
3. On the viscosity of the blood.

When two fluids, one of which, like mucilage or syrup, is viscous and the other, like water, is non-viscous, are forced through capillary tubes of equal diameter and under equal pressures, the viscous fluid will flow much more slowly through the tubes than the non-viscous one, and the slowness of its flow will be in proportion to its viscosity. The first experiments on the relationship of the viscosity of a fluid to its circulation through the blood-vessels were made by the Rev. Stephen Hales[25] (*cf.* p. 15), but his experiments were very imperfect. Poiseuille[26] investigated the relationship of viscosity to

rapidity of flow in a very complete manner, and the subject has also been experimented upon by Matthews Duncan and Gamgee,[27] C. A. Ewald,[28] Haro,[29] and others.

The viscosity of the blood is ascertained by noting the rate at which blood will flow through the capillary tubes. Several instruments of this sort are described by Dr Determann.[30] The viscosity is increased by accumulation of carbonic acid in the blood, and therefore when the blood becomes very venous it will flow with difficulty. Oxygenation of the blood lessens the viscosity, and this accelerates the circulation.

When blood would not flow from a vein after venesection, I have found the inhalation of oxygen produce a free flow of blood almost immediately.

Increased viscosity of the blood as a cause of high arterial tension has hitherto received little attention, but it is possible that future researches may show it to be an important factor in the production of this condition.

According to Haro, the flow of defibrinated blood is quickened by heat and by oxygenation, but is slowed to a remarkable extent by bile salts.

LITERATURE.

[1] Marey, *Physiologie médicale de la Circulation du Sang*, 1863 (Paris: Delahaye); *Mouvement dans la Vie*, 1868 (Paris: Bailliere); *Trauvaux du Laboratoire*, Année 1875-6, p. 337 *et seq.* (Paris: Masson); *La Circulation du Sang à l'État physiologique*, etc., 1881 (Paris: Masson).

[2] Marey, *Circul. du Sang*, p. 117.

[3] Marey, *op. cit.*, p. 618.

[4] Roy and Adami, *Practitioner*, 1890, vol. xliv., p. 242.

[5] Marey, *Circul. du Sang*, p. 152.

[6] Marey, *Physiol. med.*, etc., 1863, p. 178 *et seq.*

[7] Dudgeon, *London Med. Rec.*, 1881, p 400.

[8] A. Jacquet, *Ztschr. f. Biol.*, 1891, vol. xxviii., New Series, vol. x., p. 1.

[9] Kronecker, *vide* Scholtyssek, *Arch. f. Anat. u. Physiol., phys. Abtg.*, 1909, p. 326.

[10] Marey, *Circul. du Sang*, pp. 512 and 513.

[11] Lauder Brunton, *Med. Phys. and Circ.*, 2nd July 1879.

[12] James Mackenzie, *Diseases of the Heart*, pp. 69 and 101 *et seq.*, 1908 (London: Froude, and Hodder & Stoughton).

[13] Tigerstedt, *Handb. d. Phys.*, p. 386.

[14] Marey, *Circul. du Sang*, p. 226, with literature, 1881 (Masson: Paris); Waller, *Journ. of Physiol.*, August 1880, vol. iii., p. 37, and *Introduction to Human Physiol.*, p. 8, 1891 (London: Longmans), where a figure shows at a glance the time-relations of the pulse in different arteries.

[15] *Vide* Hirschfelder, *Diseases of the Heart*, p. 86, for bibliography.

[16] Marey, *Circul. du Sang*, p. 26; and *Travaux*, vol. i., p. 47.

[17] Burdon-Sanderson and Page, *Journ. of Physiol.*, 1879-80, vol. ii., p. 384; *ibid.*, 1883, vol. iv., p. 327.

[18] Waller, *Journ. of Physiol.*, 1887, vol. viii., p. 229.

[19] Einthoven, *Ann. d. Physik.*, 1903, Fourth Series, vol. xii., p. 1059; *Pflüger's Archiv*, 1903, vol. xcix., p. 472; and other papers quoted by Kraus and Nicolai.

[20] Electro-cardiograms. The whole subject is discussed at length, and a full bibliography given by F. Kraus and G. Nicolai, *Das Elektro Kardiogramm*, 1910 (Leipzig : Veit & Co.).

[21] Kraus and Nicolai, *Das Elektro Kardiogramm*, p. 201 ; Nicolai, *Nagel's Handb. d. Physiol.*, 1909, Bd. i., p. 825.

[22] Kraus and Nicolai, *op. cit.*, p. 147.

[23] Wright. For other methods, see Sahli, *Lehrbuch d. Untersuchungs Methoden*, 2nd ed., 622 *et seq.*, 1899 (Leipzig and Vienna : Deuticke).

[24] For conditions altering the rate of coagulation, see Schäfer in Schäfer's *Textbook of Physiol.*, vol. i., p. 145 *et seq.* (Edinburgh and London, 1898).

[25] Stephen Hales *Statical Essays*, containing Hæmastaticks, etc., vol. ii., p. 143, London. Printed for W. Innys, R. Manby, and T. Woodward, 1733.

[26] Poiseuille, *Mém. presèntés par divers Savants a l'Acad. de Sciences*, 1846, vol. ix., p. 514.

[27] Gamgee and Matthews Duncan, *Journ. of Anat. and Physiol.*, 1871, vol. v., p. 155.

[28] C. A. Ewald, *Arch. f. Anat. u. Physiol.*, *physiol. Abtg.*, 1877, p. 208 *et seq.*; *ibid.*, 1878, p. 536.

[29] Haro, *Compt. rend.*, 1881, vol lxxxiii., p. 696.

[30] Determann, *Die Viscosität des menschlichen Blutes*, 1910 (Wiesbaden : Bergmann).

CHAPTER VII

PATHOLOGY OF THE CIRCULATION

Nutrition of the Heart—Quality of Blood—Inflammation — Endocarditis — Pericarditis — Myocarditis—Fatty Degeneration — Circulation in the Heart—Blocking of Coronary Arteries—Self-massage of the Heart — Nutrient Action of Cardiac Tonics—Self-massage of the Arteries—Effect of Feebleness of the Heart on the Nutrition of the Blood-vessels—Feeble Pulse—Effect of Emotion on the Vagus Nerve—Nervous Depression—Fatty Degeneration — Pulse-rate —Effect of Position on the Pulse—Effect of Temperature—Effect of Emotion—Tachycardia—Paroxysmal Tachycardia—Exophthalmic Goitre—Bradycardia—Paroxysmal Bradycardia—Stokes-Adams' Syndrome —Intermittent and Irregular Pulse—Coupled Beats —Bigeminal Pulse—Extra Systoles—Pulsus Paradoxus and Riegel's Pulse.

Nutrition of the Heart.—The power of the heart to contract quickly and powerfully depends, like that of the skeletal muscles, on its nutrition, and this is regulated to a great extent both by the quality and quantity of blood it receives. The heart is like the priests of old, who took the best parts of the offerings before the remainder was distributed to the people. For the coronary arteries leave the aorta just above the sigmoid valves, and consequently they get the first

portion of blood as it comes fully arterialised from the lungs, and, as Sir R. Douglas Powell has pointed out, the heart is more dependent than other organs upon proper pulmonary aeration.

Quality of Blood.—Although Kronecker has shown that the heart may beat a long time without any fresh supply of oxygen,[1] yet nevertheless it uses up oxygen rapidly, and is very sensitive to lessened supply of oxygen. In experiments on the excised mammalian heart, I have seen the beats become feebler as soon as the oxygen in the nutritive fluid became less. It is even more sensitive to the accumulation of CO_2, and if this is not removed the heart's beats may become irregular, occur in groups, and finally the heart stops in diastole.[2] If the quality of the blood is bad the heart suffers. Thus, fatty degeneration of the heart is found in acute and chronic anæmia, in old age, in failing nutrition from disease, and from various poisons, *e.g.*, in chronic alcoholism, or after the administration of chloroform, arsenic, or phosphorus.

Inflammation of the Heart. Endocarditis. Pericarditis. Myocarditis.—The common cause of inflammation, either of the heart or pericardium, is infection by some pathogenic microbe. Endocarditis occurs most frequently in connection with rheumatic fever, which is probably a microbic disease, although a microbe has not certainly been identified with it. Other microbes which commonly cause it are various kinds of cocci and bacilli.[3] The inflammation of the endocardium which they produce may lead to vegeta-

tions on the valves, and consequent incompetence, and in the pericardium may produce effusion or lead to adhesions. The bacteria probably act not only mechanically by their presence in the tissues, but by the ferments they excrete and the toxins they produce. Some of them, especially the microbes of diphtheria and influenza, seem to have a special power of weakening the myocardium and sometimes paralysing the vagus. The muscular fibres of the heart become changed by the prolonged action of toxins, and undergo fatty or fibrous degeneration with consequent weakening of their contractile power.

Frequent causes are the toxins which occur in various diseases, especially those of the infective fevers. Sometimes these toxins, instead of producing fatty degeneration, cause a general softening of the muscular tissues, or parenchymatous degeneration, in which the muscular cells become degenerated but not fatty.

Circulation in the Heart.—The right coronary artery supplies chiefly the right side of the heart, the left coronary artery supplies the left auricle and ventricle and also part of the right ventricle. The terminal branches of the two coronary arteries communicate, but not freely enough to maintain circulation if one of the arteries be closed, although no doubt differences in this respect exist in different animals, and probably in different men.[4]

Blocking of Coronary Arteries.—When the circulation in the heart is suddenly obstructed by ligature or embolism of the coronary arteries the heart ceases to beat, but the mode in which

it does so differs according to the nature of the obstruction.[5] If the coronary artery is ligatured, the ventricle stops in a state of fibrillation. If the vein is ligatured the ventricle stops, but there is no fibrillation. If embolism is produced by the injection of melted paraffin into either the whole coronary arteries or into their peripheral branches, fibrillation occurs; but it does not do so if the injection is made only into the trunk of the coronary arteries and prevented by ligature from reaching the peripheral branches. The phenomenon would thus seem to be of a reflex nature, arising in the peripheral vessels.[6] When one artery is closed very slowly the communication with the other may gradually become sufficiently increased to maintain the circulation after the first has become completely occluded; and the vessels of Thebesius, at least in the dog, may maintain the circulation even after both coronary vessels have been obstructed.[7]

Partial blocking of a branch of a coronary artery may produce a local necrosis of the cardiac wall, causing either sudden death or the formation of a fibrous patch.[8] When the coronary arteries undergo gradual closure, the muscular tissue they supply undergoes either fibrous change or fatty degeneration. In either case the heart is much weakened; and in chronic valvular disease, as also in old people, brown atrophy is common.

If one artery be narrowed by atheroma, that part of the heart which it ought to nourish is apt to undergo fatty or fibrous degeneration,

and one can readily see that, even if the artery remains of its proper size, it may become relatively too small for a heart which has undergone hypertrophy.

Self-massage of the Heart. Effect of Feebleness of the Heart on its own Nutrition.—In speaking of the venous circulation in the limbs, I mentioned that the muscular movements tend to aid the return of venous blood, and the same thing occurs in the heart; for during diastole the arteries are filled at high pressure with blood from the aorta, and at the same time venous blood is pressed out of the coronary vein. The same thing probably happens also with regard to the lymphatics, which run alongside of the coronary arteries.

As Brücke mentioned in one of his lectures, which I heard in Vienna in 1867, Purkinje found that the pericardium may be likened to a bell-jar, the walls of which are more or less rigid, the pericardium being attached to the tissues all round it.[9] When the ventricle contracts, it tends to produce a vacuum in the pericardium, and thus not only to suck blood into the auricles, but also to exert suction upon the ventricle itself, and thus to draw plasma from the blood-vessels into the cardiac muscle, and also lymph into the pericardial space (Fig. 51). When the heart dilates again in diastole it tends to press the lymph out of the pericardium, and thus keeps the pericardium always moist, without any accumulation of fluid occurring. The alternate contraction and dilatation of the heart thus keep up what we may term a sort of self-

massage, by which both the circulation of blood and of lymph in and around it are properly maintained. It is evident, therefore, from what I have just said, that the maintenance of the heart's nutrition depends greatly upon its own activity, and this is a point of extreme practical importance.

Nutritive Action of Cardiac Tonics.—We can thus see that, in cases where the nutrition

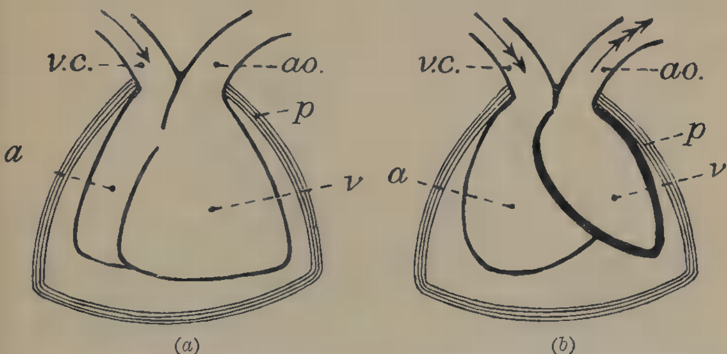


FIG. 51.—Diagram of Purkinje's experiments. (*a*) Shows the heart in diastole with full ventricle and empty auricle. (*b*) Shows it in systole with empty ventricle and full auricle. In both figures *a* is the auricle, *v* the ventricle, *vc* the vena cava, *ao* the aorta, and *p* the pericardium.

of the heart is failing, drugs which stimulate it to increased action do not act merely temporarily as cardiac stimulants, but that they are really at the same time cardiac nutrients. It is because of this fact that the good effects which we see from the use of strychnine, digitalis, strophanthus, caffeine, etc., in cardiac disease do not cease when the drugs are withdrawn, but may continue and increase, these drugs having

given a temporary increase to the power of the cardiac muscle which has enabled it to nourish itself more efficiently.

Self-massage of the Arteries.—A very important set of vessels in the body are the *vasa vasorum*, the blood-vessels which supply other blood-vessels. When these undergo change, so that the blood-vessels themselves are badly nourished, the condition of the circulation generally becomes very precarious, for there is a great deal of truth in the old saying, that "a man is as old as his arteries." When

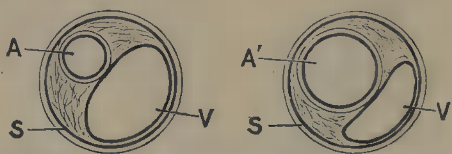


FIG. 52.—Artery and vein in common sheath, to show the effect of the arterial pulse in aiding venous circulation. A, artery in diastole. V, distended vein. S, common sheath. A′, artery distended by the cardiac systole. V′, the vein compressed and partially emptied of blood.

his arteries become atheromatous or calcareous, the termination of the man's life is not likely to be very far off. But the arteries also have a power of self-massage. The hard fibrous tissue which forms their sheath usually envelops not only the artery and vein, but also the lymphatics. Between the intima and media of the artery, and probably in the media itself, there are lymphatic spaces, and in the adventitia there are distinct lymphatic vessels. The alternate distension and relaxation of the arterial wall at each pulsation not only drive blood and lymph towards the heart at each beat

of the heart, but, during the diastole, as the blood runs out of the artery, there is a tendency for the arterial coats to separate from one another, and thus draw in fresh supplies of blood into the vasa vasorum, and of plasma from them into the arterial walls.

Effect of Feebleness of the Heart on the Nutrition of Blood-vessels.—From what I have said regarding self-massage of the arteries, veins, and lymphatics within their common fibrous

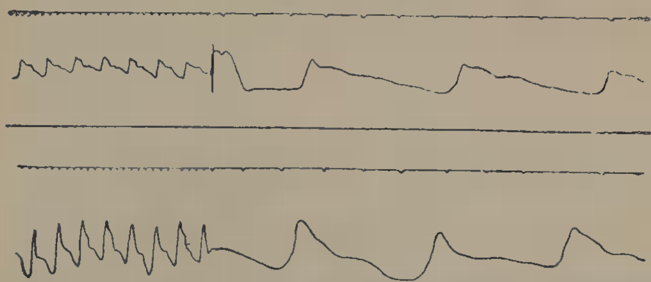


Fig. 53.—Pulse tracing, showing the effect of massage and graduated movements. Each tracing is taken partly with a slow and partly with a quick movement of the sphygmograph. The upper shows high tension and a feeble heart; the lower shows less tension and a stronger heart. These tracings I owe to the kindness of Dr Gustav Hamel, to whose treatment I had recommended the patient.

sheath, it is evident that smallness of the pulse-wave and imperfect expansion of the artery tends of itself, whether it be due to feebleness of the heart, high tension, or rigidity of the artery, to lessen the massage and to interfere both with the nutrition of the vessels and with the onward passage of venous blood and lymph. On the other hand, if the alternate dilatation and contraction of the artery at each pulse be extensive, as in the lower tracing, the self-massage will be well effected (Fig. 53). Baths, exercises, general

massage and drugs, which increase the amplitude of the pulse, are therefore useful aids to the nutrition of the arteries. Digitalis and its congeners increase the amplitude of the pulse by strengthening and slowing the heart; vascular dilators, like the nitrites, do so by diminishing the tension.

Feeble Pulse.—The chief cause of feebleness of the pulse is weakness of the heart, and this may be due to many causes. It may occur temporarily from want of food or, more permanently, from disease of the digestive organs. The heart may be feeble from dilatation or from fatty degeneration, the supply of blood to it may be lessened by mitral obstruction, or its propulsive action on the blood may be impaired by mitral regurgitation. Or its beats may be weakened by over-action of the inhibitory nerves (*vide* p. 64).

Effect of Emotions on the Vagus Nerve.—One common and important cause of a weak pulse is nervous depression, through the vagus nerve. Nearly all the emotions can be expressed in terms of this nerve. We say that the man's heart sinks within him for fear or apprehension, it beats high with joy or hope, he sighs for grief; the stomach is affected, and vomiting may ensue from disgust; the bowels move with compassion; and the effect upon the kidneys from simple excitement is well known to all those who have had to do with examinations.

As Gaskell has shown, stimulation of the vagus may produce slowing of the heart's action or feebleness of action. These may occur

separately or together, and this probably occurs also from depressing emotions.

On one occasion I was feeling the pulse of a patient in whom the pulse-rate was usually very steady. The pulse was 72, when a telegram was brought to my patient announcing the death of a relative. The pulse-rate at once fell to 66 and continued at this for several minutes, after which it again rose to 72. The strength of the pulse, as far as I could detect, remained unaltered.

In most cases, however, I believe that depressing emotions affect the strength rather than the rate of the pulse. The effect of exciting emotions is described at p. 163.

Nervous Depression. — Nervous depression from emotional causes is, I believe, a much more potent factor in disease of the circulation than is generally recognised. The effect of grief, worry, and anxiety upon the circulation, especially in elderly people, is sometimes very marked. Not long ago I saw a man whose heart was very much diseased indeed, as shown by physical examination, but he displayed wonderfully few symptoms until he was told the actual condition of his circulation, when he seemed, to use a common expression, "to take it to heart," and from that moment he went down steadily and rapidly, and died within a few days. The coincidence was very marked, as the change in him occurred within a couple of hours, so that one could hardly ascribe it to anything else than nervous depression. Conversely, hope and joy are most potent factors in

stimulating the cardiac action, and thus increasing the circulation throughout the body, and putting into action all those subsidiary aids to the nutrition of the vessels, and the return of venous blood and lymph, of which I have already spoken.

One can plainly see that long-continued depression of the heart's action by grief may bring about a condition of malnutrition with no very definite organic change to explain it; and such a condition is indeed frequently noticed, not only in the old, but even in the young, where it may predispose to tuberculosis.

Fatty Degeneration.—Another very frequent cause of weakened cardiac action is degeneration of the muscular structure itself, fibrous or fatty. This occurs very often in diphtheria, typhoid fever, and other infective diseases (p. 152). It may also occur from altered nervous supply; and Eichhorst[10] observed fatty degeneration in the heart of fowls, and Wassilieff[11] in that of rabbits, after section of the vagi. Section of one vagus was found by Fantino and Timofeew[12] to produce not fatty but atrophic degeneration, and the part of the heart affected varied according as the right or left vagus was divided. Probably the great weakness of the heart after diphtheria is due in some cases to a triple action, viz., (1) to the effect of the toxin in causing degeneration of the cardiac muscles; and (2) to its causing degeneration of the suprarenal bodies; and (3) to its effect in producing paralysis of the vagus nerves, just as it does of the nerves going to

the pharynx. This paralysis is shown by the extreme rapidity of the pulse, which may come on during the height of the disease and continue for months afterwards.

Fatty or fibrous degeneration of the muscular fibres naturally produces feeble action of the heart, and such degeneration is commonly consequent upon interference with the circulation through the coronary arteries. Here we must distinguish between the two sides of the heart, because although both coronary arteries may be affected, yet occasionally we find one affected and not the other. The symptoms due to affection of the two sides we shall have to consider later on. It is to be noted that sometimes fatty degeneration may occur in patches, affecting the trabeculæ, or the musculi papillares.[13] When the latter are affected it seems highly probable that the conduction of stimuli in the ventricle may be impaired.

Pulse-rate.—The rate of the pulse depends on many factors. In disease it may be much affected by the condition of the heart itself; but in health it is regulated chiefly by the central nervous system through the cardiac nerves, and especially by the vagi. These nerves are in a state of tonic action, which may be increased or diminished so as to slow the pulse or quicken it. Such alterations occur from reflex stimuli arising from any part of the body, but the tone is maintained to a great extent by the pressure of blood within the vessels supplying the inhibitory centre in the medulla. When the tension within these vessels rises, this centre is stimu-

lated and the pulse slowed; when the tension is diminished, the centre acts more feebly and the pulse becomes quicker. In consequence of this any rise in the blood-pressure generally, as from exposure to cold or locally from position, tends to slow the pulse.[14]

Effect of Position.—The usual pulse-rate in man is sixty to eighty per minute in the sitting position, and rather quicker in women. The effect of gravity tends to make the blood sink from the head to the feet, and it is probably on this account that the pulse in the upright posture is usually about eight beats quicker, and in the recumbent position about four beats slower than in the sitting posture.[15] These numbers vary much in different persons, and in the same person at different times; but usually there is a difference of at least seven beats between lying and standing, and the absence of this difference has been regarded by Huchard as evidence of the rigidity of the arteries.[16]

When the head is brought lower than the body some accelerating mechanism is brought into action, for I have found, in experiments on myself, that while my pulse conforms to the rule in sitting, standing, or lying down, it becomes much quickened if I lie with my head hanging down. I have seen the same condition in a case of cerebral abscess, where the pulse was very quick before the operation, but fell to the normal when the intracranial pressure was removed by trephining.

Effect of Temperature.—Warmth quickens the pulse-rate,[17] both by acting directly on the

heart[18] and by dilating the vessels, lowering the blood-pressure, and thus lessening the stimulation of the vagus roots.[19] Cold has an exactly opposite effect on the heart and vessels, and slows the pulse.

In fever the high temperature of the body quickens the pulse, but sometimes other factors, such as toxins, may modify the effect of temperature, so that in typhoid fever the pulse is usually much slower than one would expect from the temperature.

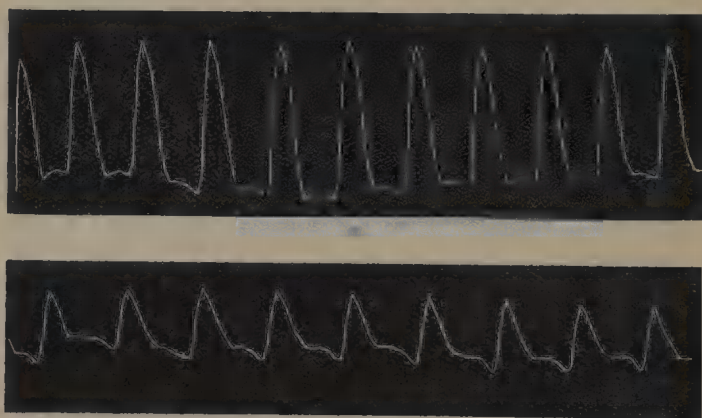
Effect of Emotion.—Emotions may quicken the pulse very greatly, and in nervous people the mere excitement of consulting a doctor may raise the pulse to 100 beats per minute or more, while at the same time it may greatly increase the force as well as the rate of the heart's action (Fig. 54). This condition usually subsides quickly. A very common rate of pulse is 76 in normal conditions, 92 in moderate excitement or slight fever, and 120 in great excitement or high fever.

A pulse of 120 indicates that the vagus is not acting, for this rate has been found when the vagus has been paralysed by atropine.[20] I have seen it occur more or less permanently when the vagi were paralysed after diphtheria or from alcoholic neuritis.

Tachycardia.—After very severe exercise the heart may remain quick for several days. A very quick pulse without obvious cause ought to lead to careful examination for myocarditis.

Paroxysmal Tachycardia.—This is a condition in which the pulse becomes suddenly

quickened to twice, thrice, or sometimes nearly four times its normal rate, from 70 to 140, 200 or 280. After the attacks, which are usually associated with great discomfort, have lasted for a varying time from minutes to days, they pass off as suddenly as they came. The excessive pulse-rate shows that they cannot be due to paralysis of the vagus alone, but that there is



b

FIG. 54.—Effect of excitement on the pulse of a nervous boy aged 15. *a* is a tracing taken immediately on his entering the consulting-room; *b* some minutes later, when his agitation was passing off.

either some excitable condition of the heart itself or great stimulation of the accelerator nerves, or both.[21] The fact that they can frequently be cut short by an emetic appears to indicate that reflex stimulation of the accelerators from the stomach is a powerful factor in their production. At the same time there is probably some predisposing cause in the heart

itself, for Lewis has produced tachycardia experimentally by ligaturing a coronary artery,[22] especially the right. Electro-cardiograms obtained during an attack seem to show the presence of auricular fibrillation. Very few have been examined after death, but in one-half of them interstitial myocarditis or fatty degeneration has been found.

Exophthalmic Goitre.—In cases of exophthalmic goitre the internal secretion of the thyroid appears not only to quicken the heart but to dilate the vessels, and in this disease the pulse frequently rises to 130 or 140 beats per minute, or even more. It would thus appear that not only is the vagus paralysed, but that the accelerators are stimulated. This effect upon the circulation is due, at least to a considerable extent, to the action of the actual secretion of the gland itself, for I have seen it occur in a patient with myxœdema who took thyroid by the mouth too frequently and too long.

Bradycardia or Brachycardia.—This is just the opposite of tachycardia. In some people the pulse is naturally very slow. Napoleon's pulse is said to have been only 40 per minute, and in a fellow-student of mine it was only 42.

The slow pulse may be either apparent or real. In some cases an apparent slowness is due to the fact that some beats of the heart are so feeble that the ventricle never opens the aortic valves, and no pulse reaches the wrist. Sometimes alternate beats are weak and strong, so that for a heart beating eighty times per minute only forty radial pulses are felt[23] (Fig.

55). In other cases there are no small beats but only slow pulsations.

As a general rule bradycardia is probably due most frequently to excessive action of the inhibitory centres in the medulla or in the heart itself, and their action may be increased by actual weakness of the motor apparatus in the heart, so

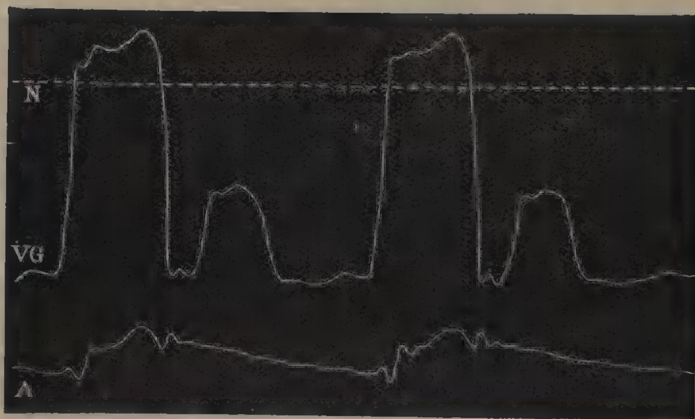


FIG. 55.—Tracings from the left ventricle and aorta, showing a slow pulse in the aorta due to each alternate beat of the ventricle being too weak to overcome the pressure within the aorta and lift the aortic valves. The upper tracing, VG, is from the left ventricle. The lower, A, is from the aorta. N is the level which the pressure within the ventricle must attain in order to raise the aortic valves. (After Marey.)

that stimuli are either slowly generated or badly conducted.

It may occur from central stimulation of the vagus by high arterial tension in Bright's disease, or lead-poisoning; or intracranial pressure in cerebral tumour, or apoplexy; and by chronic inflammation, as in general paralysis. It occurs also in mental affections, as mania and

melancholia, and in disease or injury of the medulla itself or of the cervical cord. It may be caused by reflex stimulation of the vagus from the sexual organs, skin, liver, or stomach, as in dyspepsia,[24] gastric ulcer, or cancer, for reflex stimulation of the vagus may occur from stimulation of any sensory nerve.[25]

Heart-block may cause it, so that the ventricles contract only once for every three or four beats of the auricles.[26] Sometimes the inhibitory mechanism in the heart itself may be excited by irritation of the vagus trunks or branches of the vagus in the cardiac plexus, just as slowness of the pulse may be produced experimentally by irritation of the vagus in animals. Slowness of the pulse sometimes occurs in women after childbirth, but the explanation of it is uncertain. It is very apt to occur when the heart is feeble, as during convalescence from infective diseases, such as influenza, acute rheumatism, diphtheria, pneumonia, and typhoid fever; in general weakness due to anæmia, chlorosis, and diabetes; and in permanent weakness of the cardiac walls due to fatty or fibroid degeneration. It is seen also in typhoid fever even while the temperature is high, and in this case it is probably due to the effect of a toxin which stimulates the inhibitory mechanism in either the medulla or the heart, and prevents the pulse from rising above 80 to 90, even when the temperature would lead one to expect a pulse of 100 to 120. In the convalescence from diphtheria the slowness of the pulse is not improbably due to some neuritis of the vagus, which,

in severe cases, leads to complete paralysis with exceedingly rapid pulse. Other poisons, such as those which occur in uræmia, and also alcohol, coffee, digitalis, lead, and tobacco, may cause a very slow pulse. It is frequent in jaundice, and its occurrence here appears to be due to the bile acids, which weaken the cardiac muscle and render it more easily affected by the inhibitory nerves.

Paroxysmal Bradycardia.—In this affection the pulse suddenly becomes slow and usually small and weak. This condition may only last for a few minutes or may continue for hours or even days, and then passes off again suddenly. It is usually accompanied by coldness and paleness of the skin, perspiration and feelings of giddiness and faintness. It occurs in patients whose hearts are enfeebled by infective diseases, as acute rheumatism, pneumonia, and especially influenza, or by chronic myocarditis, fatty heart or sclerosis of the coronary arteries. But whilst these conditions predispose, the actual attack is probably due to excessive action of the vagus, caused by some reflex irritation, especially from the stomach or intestines. Certain poisons give rise to it, especially tobacco, and sometimes coffee or tea, though these latter more usually produce tachycardia.[27]

Stokes-Adams' Syndrome.—This consists of extreme bradycardia (Fig. 56) associated with fainting or convulsions. It is generally due to heart-block associated with lesions of His's bundle, but the attack may be brought on by action of the vagus. The two factors may be

separated by giving atropine (1 mgm. = $\frac{1}{60}$ gr. troy). This paralyses the vagus and removes the slowness of the pulse if it is entirely due to

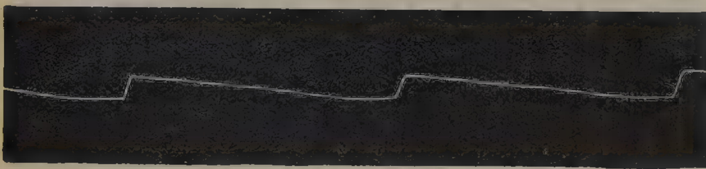


FIG. 56.—Very slow pulse. (From a Stokes-Adams case.

the vagus, relieves it if it is partially due, and does not affect it if it is caused entirely by heart-block.[28]

Intermittent and Irregular Pulse.—Intermission of the pulse is a frequent condition. In it one beat is occasionally dropped. This may happen once in three times, so that 2 regular beats come followed by a pause, or it may occur after 4, 5, or more beats which are quite regular, or it may happen at irregular intervals; for example, once after 3, next time after 5, next after 7, and then again after 2. A condition very like that of imperfect heart-block was produced by Erlanger in his experiments.[29]

Coupled Beats.—In pulse tracings sometimes two beats occur with a short interval between them, the second being followed by a somewhat longer interval. To this condition the term bigeminal pulse is often applied, and when the interval occurs after three or four beats they are called trigeminal or quartogeminal. Wenckebach objects to the term as misleading, and would discard it in favour of the term extra

systole. It occurs in cases of poisoning by digitalis or tobacco. The irregularity from tobacco is sometimes very extraordinary: one slow, strong beat followed by a number of very quick ones.

This condition may also occur quite apart from tobacco, and may persist for many years without really affecting the patient's health. One patient of mine, who is now seventy-nine years of age, had for many years a bigeminal pulse, that is, two beats in rapid succession followed by a longer pause. He is still hale and healthy.* A relative of my own died at the age of eighty-four, after having had a very irregular pulse for sixty-seven years. This irregularity of the pulse came on after an attack of rheumatic fever at the age of seventeen, and continued all the rest of her life. It is impossible to give with certainty any explanation of the exact cause of these forms of irregularity. Some of them, such as irregular bradycardia or occasional intermission of a beat, appear to be due to heart-block.

Bigeminal Pulse. — Bigeminal pulse may sometimes occur without any other apparent cause than nervousness, as is shown by the tracings which I here append, where the pulse assumed a bigeminal character while the sphygmograph was still upon the wrist and

* The irregularity came on in 1884. My tracings of his pulse are reproduced, but inaccurately, in my article on "Nervous Diseases of the Heart" (Hare's *System of Practical Therapeutics* (Philadelphia and New York), 2nd ed., 1901, vol. ii., p. 375).

between the taking of two tracings. There was no alteration in the cardiac dulness and no murmurs were present, but the tension was somewhat low, 108. I have here used the word "bigeminal" in its common acceptation, but the subject of different forms of it has been discussed by Lewis in his book on the Heart, p. 249. Bigeminal pulse may also be produced by the inhalation of nitrite of amyl.

Extra Systoles.—The occurrence of ventri-

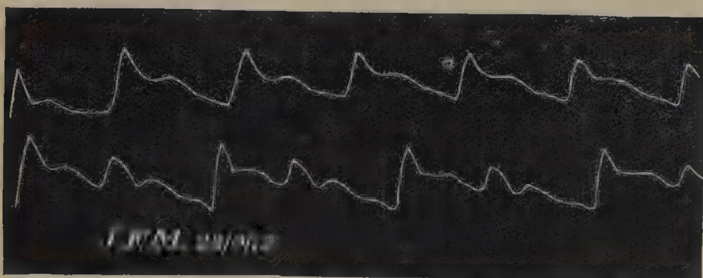


FIG. 57.—Bigeminal pulse coming on while the sphygmograph was upon the wrist. The upper tracing represents the normal. The second was taken almost immediately after the first. There was no apparent reason for the alteration. The patient was a youth, aged 19, suffering from albuminuria. Tension 108 mm.

cular extra-systoles which do not reach the pulse (*vide* p. 165) may explain many cases of intermission and irregularity; but the question at once arises, What causes the extra-systoles? In experiments on mammals they are usually produced by electrical or mechanical stimulation of the exposed ventricle itself, or of the pericardium; but they also occur in a heart completely isolated, artificially perfused if the pressure is suddenly raised either in the aorta or pulmonary artery.[30]

The extra-systole starts from the left ventricle when the outflow from the aorta, and from the right ventricle when the flow from the pulmonary artery is stopped.[31] At present it is impossible to be sure whether this result is due to the stimulus of pressure acting on the cardiac muscle only, or also on the cardio-motor and inhibitory mechanism contained in it.

In man the heart can be stopped by raising the pressure in the lungs, and thus obstructing the flow through the pulmonary vessels; as in Valsalva's experiment by forcible expiration against resistance. Such obstruction will occur, though to a lesser degree, in violent coughing. The tension in the aorta may be suddenly raised by any violent exertion, and as the breath is frequently held in straining, pressure may be increased in both ventricles.

While such experiments clearly show that irregularity may arise from conditions affecting the heart alone, without intervention of the nervous system, it must be remembered that the vagus is easily stimulated reflexly, and it is possible that such stimulation may aid at least in production of intermittence. I think a true explanation of all cases of irregularity is only obtainable by assuming that the nervous system also affects the cardiac rhythm, and that sometimes nervous and muscular rhythms interfere with one another. In Chapter I., I mentioned some grounds for this belief, and the experiments by von Basch and Fröhlich tend to confirm the accuracy of my views.

Pulsus Paradoxus and Riegel's Pulse.—These

forms of irregularity usually indicate pleuro-pericardial adhesions, which probably cause tugging at the heart during respiration. The pulsus paradoxus is a diminished size of the pulse or dropping of a beat during inspiration,[32] whilst in Riegel's pulse these phenomena occur during expiration.[33]

LITERATURE.

1 Literature by Handler, *Zeitschr. f. Biol.*, 1890, p. 233.
2 Albanese, *Arch. f. exper. Path. u. Pharm.*, 1893, vol. xxxii., p. 302.
3 Ziegler, *Lehrbuch d. Pathologischen Anatomie*, 8th ed., vol. ii., pp. 30 and 43 (Jena: Fischer, 1895).
4 Baumgarten, *Amer. Journ. of Physiol.*, 1899, vol. ii., p. 251.
5 Old literature regarding ligature of a coronary artery is given by W. T. Porter, *Journ. of Physiol.*, 1894, vol. xv., p. 120 *et seq.;* also by Tigerstedt in his *Lehrbuch*, p. 190. See also Schäfer's *Textbook of Physiol.*, 1900, vol. ii., p. 164; and Nicolai, *Nagel's Handbuch. d. Physiol.*, 1909, vol. i., p. 694.
6 Kronecker, *Physiol. Cong. III.*, in Bern, 1893.
7 Pratt, *Amer. Journ. of Physiol.*, 1898, vol. i., p. 86.
8 Baumgarten, *Amer. Journ. of Physiol.*, 1899, vol. ii., p. 243.
9 Purkinje, *Breslau Schles. Gesellsch. Uebersicht*, 1843, p. 157 *et seq.*
10 Eichhorst, *Die trophischen Beziehungen der Nervi Vagi zum Herzmuskel*, p. 18 (Berlin, 1879).
11 Wassilieff, *Ztschr. f. klin. Med.*, 1881, vol. iii., p. 316.
12 Fantino and Timofeew quoted by Tigerstedt, *Lehrbuch*, p. 257.
13 Ziegler, *op. cit.*, p. 36.
14 For experiments and literature on this subject, *vide* Tigerstedt, *op. cit.*, p. 300 *et seq.;* also, François Franck, *Trav. du lab. de Marey*, 1877, vol. iii., p. 276.

15 Guy, article "Pulse," in Todd's *Cyclopædia of Anat. and Physiol.*, p. 185 *et seq.*, 1852.

16 Huchard, *Maladies du Cœur*, 3me ed., vol. i., p. 90 (Paris: O. Doin, 1899).

17 Lauder Brunton, *St Bartholomew's Hospital Reports*, 1871, vol. vii., p. 216 *et seq.* (the older literature is given here); also, *Journ. of Anat. and Physiol.*, 1876, vol. x., p. 602.

18 Gaskell, *Phil. Trans.*, 1882, p. 993.

19 Hewlett, *Heart*, vol. ii., p. 237.

20 von Bezold and Bloebaum, *Untersuch. a. d. Phys. lab.*, Würzberg, 1867, vol. i., p. 1 *et seq.*

21 Martius, *Tachycardie* (Stuttgart, 1895); Hirschfelder, *Diseases of the Heart and Aorta*, 1910, p. 572, gives bibliography.

22 Lewis, *Heart*, vol. i., p. 98 *et seq.* (London, 1910).

23 Marey, *Circul. du Sang*, p. 122 (Paris, 1881).

24 Somerville, with commentary by Lauder Brunton, *Practitioner*, 1876, vol. xvi., p. 186.

25 *Vide* Tigerstedt, *op. cit.*, pp. 287, 288, 289.

26 Gibson, *Nervous Affections of the Heart*, p. 61 (Edinburgh: Pentland, 1904); Mackenzie, *Study of the Pulse*, pp. 97, 213, 288 (Edin. and London: Pentland, 1902).

27 Hirschfelder, *op. cit.*, pp. 48 and 460.

28 Osler, *Angina Pectoris and Allied States*, p. 70 *et seq.* (New York, 1897); Hirschfelder, *op. cit.*, p. 460 *et seq.*

29 For discussion of arhythmia, its varieties and causes, *vide* Wenckebach, *Arhythmia of the Heart*, translated by Snowball, 1904 (Green, Edin. and London); J. Mackenzie, *The Study of the Pulse*, 1902 (Pentland, Edin. and London); Vaquez, *Les Arhythmies*, 1911 (Baillière et Fils, Paris); Lewis, *Mechanism of the Heart Beat*, 1911 (Shaw & Sons, London).

30 Heidenhain, *Pflüger's Archiv*, 1872, vol. v., p. 143.

31 H. E. Hering, *Pflüger's Archiv*, 1900, vol. lxxxii., p. 1; Martin, *Phil. Trans.*, 1883, vol. clxxiv. (2), p. 213; Howell and Donaldson, *Phil. Trans.*, 1884, vol. clxxv., p. 151.

32 Griesinger, *vide* Hirschfelder, *op. cit.*, 2nd ed., p. 604.

33 Riegel, *Berlin klin. Wochenschr.*, 1877, Jg. xiv., 657.

CHAPTER VIII

SYMPTOMS OF DISORDERED CIRCULATION

Palpitation — Effect of Position on Palpitation — Abdominal Pulsation—Throbbing of Arteries—Flushes of Heat—Shock—Shock in Surgery—Shock from Gastric Disturbance—Syncope—Low Blood-pressure — Breathlessness — Headache — Migraine — Sensibility of Arteries—Functional Sensory—Functional Motor Phenomena — Sensibility of the Heart — Pain in the Cardiac Region — Angina Pectoris —Pathology of Angina Pectoris — Claudication and Angina Pectoris — Views of Allen Burns — Views of Sir Benjamin Brodie—Angina Abdominis—Cardiac Dyspnœa—Raynaud's Disease—Chilblains; Urticaria; Angio-neurotic Œdema — Atheroma — High Blood-pressure — Insomnia — Giddiness — Senile Rise of Pressure—Senile Decay—Embolism and Thrombosis.

Palpitation.—Palpitation of the heart is a very troublesome symptom, and its causation is very obscure. Sometimes it appears to be an almost purely subjective sensation, as the patient has a sensation of the heart beating strongly, yet the hand applied to the apex beat does not perceive anything unusual. In other cases the force of the apex beat, as felt by the hand, is distinctly increased. I have noticed such an increase take place in animals poisoned

by digitalis. In my thesis on the action of this drug I discussed the mechanism of palpitation, and arrived at the conclusion that it was probably due to increased power of the heart in proportion to the resistance it had to overcome, so that the ventricular contraction occurred rapidly, and the apex, therefore, struck forcibly against the chest wall.[1] What seems to confirm this opinion is the fact that palpitation is frequent in states of debility, but is frequently, indeed one may say generally, absent when the heart is hypertrophied but the tension is high; so that, despite its abnormal strength, the heart cannot contract quickly.

Effect of Position on Palpitation. — One would naturally expect that a constantly recurring rhythmic blow upon the heart at each pulsation would increase its action, and, as a matter of fact, this appears to be the case. The heart is a mobile organ and moves considerably to the left when a person lies on that side. The apex, therefore, tends to strike more forcibly against the chest wall, and as the effect of this is similar to that of a blow on the heart at each beat, many people are unable to lie on the left side in consequence of the palpitation which then comes on, while if they lie on their right side the heart rests on the right lung as on a cushion, and they become quite comfortable. When the stomach is distended by flatulence it tends to push the heart up and bring its apex against the chest wall, with the same result as lying on the left side, and when the flatulence is expelled and the heart resumes

its normal position the palpitation disappears (*cf.* Fig. 73, p. 226).

Abdominal Pulsation.—In this condition the abdominal aorta throbs violently, so much so that it is sometimes visible through the abdominal walls and gives rise to the suspicion of aneurism.* The pulse is, however, only forwards and not lateral, and is lessened or removed when the patient leans forward. It is in all probability due to a loss of tone in the abdominal aorta (p. 84), and frequently occurs in connection with some irritation in the abdomen, such as gastric or duodenal ulcer.

Throbbing of the Arteries.—Similar throbbing may occur in the carotid and subclavian arteries, and probably other arteries also, as patients not unfrequently complain of throbbing in the head or extremities. Such throbbing occurs frequently in connection with exophthalmic goitre.

"**Flushes of Heat.**"—Sudden sensations of heat are a very common symptom in women at the menopause. They are sometimes accompanied by visible flushing, but sometimes not. They are probably dependent upon a kind of toxæmia due to some internal secretion.

Shock. — Another important condition in which both heart and vessels appear to be affected is that of shock. Here the heart may become slow and feeble, but this does not appear to be all, for the general depression is out of proportion even to the feebleness of the heart's action. Shock is especially apt to come

* Sir James Paget's *Clinical Lectures*, p. 138 (London : Longmans).

on from a blow in the epigastrium, and Goltz, in his famous experiment, showed that if a frog be suspended in the upright position and its heart exposed, a blow upon the intestines has a two-fold action.[2] It (1) stops the heart reflexly through the vagus; but after this effect has passed off (2) the heart beats again, but is empty, and sends on no blood into the vessels, because the blow has caused dilatation of the abdominal vessels, and all the blood becomes stored up in them, so that none reaches the heart.[3]

It is not improbable that a similar effect may

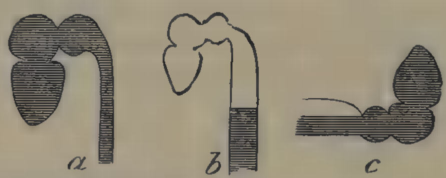


FIG. 58.—Diagram to illustrate Goltz's experiments. *a*, Normal heart in the upright position; *b*, heart in same position after shock; *c*, heart as in *b*, but in recumbent position, showing it full, so as to keep up circulation, though the veins are still dilated.

occur from irritants inside the stomach or intestine. When large quantities of alcohol have been swallowed at a draught, death has occurred almost instantly, and the mechanism of its production was probably the same as in Goltz's experiment. Severe pain from irritation of nerves in other parts of the body may stop the heart, but under ordinary circumstances it also causes contraction of the abdominal vessels, and thus keeps up the blood-pressure and maintains the circulation.[4] If the pain be very excessive, it is quite possible that an opposite

effect may be produced, and thus fatal syncope may ensue.

Shock in Surgery.—In surgical operations if anæsthesia is imperfect, reflex stoppage of the heart may occur without reflex contraction of the vessels, and thus fatal shock may be produced, whilst perfect anæsthesia would have abolished any reflex action on the heart as well as on the vessels, and thus prevented any danger.[5]

Shock from Gastric Disturbance. — A very remarkable case of shock from apparently a very slight cause occurred in one of my patients. He dined late and had some wine, which possibly underwent acetous fermentation in the stomach. About two hours afterwards, when walking round his house before going to bed, he took a small quantity of whisky and aerated water. Immediately he felt a shock, staggered, and would have fallen to the ground had he not been supported by a servant who was accompanying him. A medical man staying in the house who came to his assistance found him pale and collapsed looking, and his pulse beating at the rate of 130 per minute. He did not recover completely for two or three hours, and marked improvement only occurred after the administration of a large dose of sodium bicarbonate, although 40 grains of bromide had been given without effect. The symptoms were precisely such as would have followed a blow on the epigastrium, and I am unable to account for them except on the supposition that the effervescence caused by the aerated water sprayed the

acid contents of the stomach all over its internal surface, while at the same time evolution of gas may have added the stimulus of mechanical distension.

Syncope.—The remarkable difference between shock and syncope is that usually in shock the brain remains clear, but in syncope the person becomes suddenly unconscious. The pathology of syncope has not been thoroughly made out, but it appears to be due to sudden anæmia of the brain. The brain requires a large supply of blood when it is functionally active, so that blood is withdrawn from the limbs, and they become smaller. This is shown by Mosso with the aid of the plethysmograph.[6] When measured by this instrument, the volume of the arm was found to become much smaller when the person thought hard, as the blood required by the increased functional activity of the brain was withdrawn from the arm. When the body is upright, the pressure of blood in the brain is less, but it becomes greater when the head is lowered. The recumbent position is therefore the best to restore a fainting person, and the tendency to faint may sometimes be averted by placing the head on the hands between the knees. Before the introduction of anæsthetics it was a frequent custom to perform operations in a state of syncope, which was induced by laying the patient flat on the ground for a short time and then raising him very suddenly to the upright position by several strong men.[7] A curious observation was made by John Hunter on the flow of blood during syncope. In a lady who was being bled,

the blood issued from the vein slowly and was black, but the moment she fainted the blood rushed out quickly and became of a bright colour. This phenomenon is exactly what is seen in the condition of the submaxillary gland when its arterioles dilate on irritation of the chorda tympani. As the blood from the veins at the bend of the arm comes to a great extent through the muscles, we are, I think, justified in believing that, in some cases of syncope at least, the vessels of the muscles undergo sudden dilatation, and thus the blood-pressure becomes enormously and instantly reduced[8] (*cf.* p. 17).

At the same time the tendency to faint in hot rooms is much greater in women than in men, yet in men the muscular area of vessels is larger and in women the splanchnic area (p. 19). It seems probable, therefore, that splanchnic dilatation may cause faintness as much as muscular.

Low Blood-pressure.[9]—The pressure is low in shock and syncope, in collapse from poisons, in severe hæmorrhage or profuse discharges from the bowel or stomach, as in diarrhœa, dysentery, cholera, or continuous vomiting. It occurs in fevers generally, especially typhoid, as a sequel to influenza and diphtheria, in fatty heart, and in debility from chronic diseases. Two conditions in which I have found the tension very low are phthisis and excessive smoking. An abnormally low blood-pressure may sometimes be a precursor of phthisis, and may possibly give early warning of danger. In one case I found an abnormally low pressure in an apparently healthy man who developed

phthisis several months afterwards. One of the most common causes of low blood-pressure is excessive smoking. A single pipe of tobacco probably raises the blood-pressure, but continuous heavy smoking certainly depresses it. It would almost seem as if in the case of tobacco-smoking anti-substances were generated in the body which more than counteracted the effect of nicotine. I am uncertain how far this lowering of blood-pressure is due to dilatation of the vessels, and how far to weakness of the cardiac action. On account of its effect upon the heart the smoking must be regulated to a certain extent, but at the same time I am rather chary of asking heavy smokers, who have at the same time a high blood-pressure, to give up smoking entirely.

Breathlessness.—In breathlessness of cardiac origin the patient is often free from any discomfort when at rest, but any exertion brings on an attack. In this condition the inspiration is usually quick, but expiration is much prolonged. Von Basch attributes this to stiffness of the alveoli in the lung, so that they fill easily but collapse with difficulty. They are in fact held open by the network of capillaries which surrounds them, and which is stiff from congestion.[10] The breathlessness may be due to backward flow of blood or impeded onward flow in mitral regurgitation or obstruction, or to inability of the right ventricle to drive the blood against resistance in emphysema or weakness of the right ventricle itself from dilatation or fatty degeneration due to atheroma of the right coronary artery[11] (p. 153).

Headache.—Headache is a common symptom in heart disease. In patients with high tension it varies from a dull ache to excruciating pain. It is usually diffused over the head, but it may sometimes be localised more in one spot than another, *e.g.* forehead or occiput, and may, like ordinary migraine, be accompanied by flashes of light. Curiously enough, there is sometimes little or no recollection of pain, though it may have been extremely great while it lasted.

Migraine.—This affection occurs quite apart from either cardiac disease or high tension. The pain usually affects one or other temple, and is frequently brought on by strain of the eyes due to astigmatism or other visual defect. Its pathology is very interesting, and, I think, throws much light on some other disorders of the circulation. A good deal of discussion has taken place in regard to the pathology of sick headache or migraine. Du Bois-Reymond described the temporal artery in his own case as being much contracted during the headache,[12] and therefore concluded this was a general condition; while others have described this artery as widely dilated and throbbing, and have supposed this condition to be constant. I have, unfortunately, had only too many opportunities of repeating these observations on my own head, and I have found that, as is often the case, both parties are right, and both parties are wrong; that the condition described by each occurs, but that it does not extend to all parts of the artery at the same time. Sometimes, for example, during a fit of migraine I have

found my temporal artery widely dilated and throbbing, at other times I have found it hard and contracted, like a piece of whipcord; but when it was dilated, if I followed it onward towards the periphery I ascertained that the ascending temporal branch was contracted like a bit of piano-wire (Fig. 59, *c*). On most occasions, if I followed the contracted temporal artery backwards towards the heart, I found that the

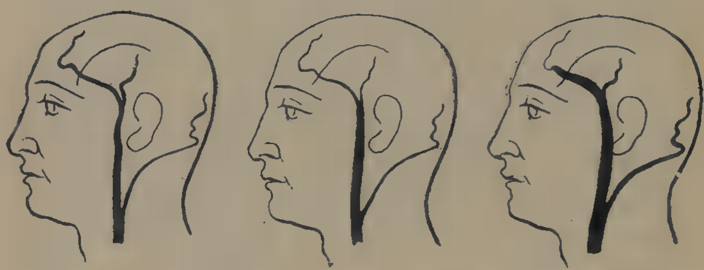


FIG. 59.—Diagrams of the carotid, temporal, and occipital arteries in migraine. *a*, In the normal state; *b*, during migraine, showing dilatation of the carotid and spasmodic contraction of the temporal arteries; *c*, during migraine, showing dilatation of the carotid and temporal arteries, and extreme contraction of the ascending frontal branch of the anterior temporal artery.

carotid on that side appeared to be as thick as my thumb, distended to three times its normal diameter, and pulsating violently. The conclusion I came to, therefore, in regard to the pathology of migraine, is that there is *peripheral contraction and central dilatation of the arteries.*[13]

Sensitiveness of Arteries. — Arteries are sensitive, as was known in olden days before the introduction of anæsthetics, because patients complained of pain when the arteries were

ligatured. That the pain in migraine is to a great extent due to the stretching action exerted on the contracted temporal artery by the blood which tries to pour into it from the dilated carotid, is shown by the fact, which I have proved in my own case, that if pressure be exerted upon the carotid so as to stop the pulse in the temporal artery, the headache will frequently disappear instantly. Unfortunately, however, it is almost impossible to compress the carotid without also pressing upon the vagus, and the sense of oppression on the chest which this produces is so great that one is generally obliged to cease compression after a few seconds, although the moment the finger is removed the pain in the head comes back with a rush of peculiar intensity. Megrim is often regarded as a neuralgic condition, but the observations upon my own head which I have just detailed have convinced me that, although the vascular disturbance which occurs in it is almost certainly due to an altered action of the vaso-motor nerves, yet the pain is to a great extent like that of colic, where we find intense pain due to spasmodic contraction of one part of the intestine with dilatation or distension of another.

Functional Sensory Phenomena.—If we assume that the arteries inside the cranium contract in the same way as outside, it is easy to understand the curious nervous symptoms that often accompany migraine. Thus, if the artery to the visual centre be contracted there will be flashes of light, zigzags, or hemianopsia.

Similar contraction of the arteries supplying the auditory, olfactory, or gustatory centres may cause disturbances of the corresponding senses.[14]

Functional Motor Disturbances. — The functions of the cerebral motor centres may be temporarily abolished by a spasm of the arteries going to them cutting off their supply of blood. This was, I believe, first recognised by Professor Emil du Bois-Reymond, who considered epilepsy and migraine to differ in degree rather than in kind.[15] I have myself observed cases in which migraine was accompanied by aphasia, and Russell has described cases of temporary hemiplegia probably due to arterial spasm.[16] In some cases of this sort it is difficult to determine how much is due to spasm and how much to partial obstruction of an artery by atheroma and possibly thrombosis.

Sensitiveness of the Heart. — Like the vessels, the heart is probably sensitive and capable of originating pain of a most intense character.[17] Pressure from the outside is not felt, as Harvey discovered in the case of young Lord Montgomery, in whom a congenital defect of the sternum exposed the heart.[18] But pressure from without, unless very excessive, does not produce pain in hollow muscular organs such as the stomach, intestines, urinary bladder, gall-bladder, gall-duct, or ureter; yet distension from within causes pain of the most intense character in all these organs. They are all liable to discomfort without pain, and the heart, too, frequently feels discomfort without pain. The sense of oppression which is felt from grief

or anxiety is, I think, due to the effect of the vagus nerve, because I have noticed in my own case that grief has produced a sensation of oppression in the chest which has persisted after the emotion which had given rise to it had passed away. We know that this feeling of oppression can be produced by mechanical irritation of the vagus, for Professor Czermak had a small exostosis on one of his cervical vertebræ, and by compressing his vagus between it and his finger he was able to stop his heart, but the pressure at the same time caused this feeling of oppression, or, as he termed it, "Beklemmung" in the chest.* [19]

Pain in the Cardiac Region.—The two chief seats of cardiac pain are over the apex and mid-sternum. In all probability mid-sternal pain is more closely connected with the condition of the aorta and irritation of the sensory nerves in it, while pain over the apex may be connected with some irritation in the cardiac muscle or in the pericardium, but it frequently occurs quite independently of any organic disease of the heart whatever. When I was a house-physician the cases under my observation were generally of a serious nature, and in them pain in the cardiac region was usually associated with organic heart disease, or else with inflammation of the pleura.

* When Professor Czermak described this feeling he supposed that the vagus was compressed between his finger and an enlarged gland, but I was informed by the late Professor Sharpey that what Czermak supposed to be a gland was afterwards discovered to be an exostosis on one of the cervical vertebræ.

When I began to see an enormous number of out-patients at St Bartholomew's Hospital (600-800 in a week), I at first carefully examined the heart in cases where complaint was made of pain over the apex; I soon found, however, that in the great majority of these cases there was nothing the matter with the heart at all, and in women, especially, it was generally associated with leucorrhœa. How far this condition is due to a nervous connection between the pelvic organs and the heart, and how far it may be due to some alteration in the condition of the blood consequent upon the discharge, I cannot say, but under treatment by iron the pain generally subsided in a very short time.

Angina Pectoris.—One of the most distressing forms of cardiac disturbance is angina pectoris. In it there are frequently two sensations, or perhaps even more: one of intense oppression, and one of extreme pain. That of extreme pain I am inclined to regard as similar to colic in the intestine, and as depending upon spasmodic contraction of the heart against resistance which it cannot properly overcome.[20] In many cases this is situated about mid-sternum, but it is frequently felt more towards the cardiac apex, and often radiates towards the shoulders and down the arms, especially the left arm.[21] As I have already said, it is probably due to a want of relationship between the power of the cardiac muscle and the resistance it has to overcome. It is brought on by anything that raises the blood-pressure quickly, such as exertion or emotion, and especially by the

emotion of anger, which, as in John Hunter's case, may bring about a fatal attack at once. Anything that interferes with the action of the heart tends to increase the pain, and thus distension of the stomach by tilting the heart up makes the patient worse, and much relief is afforded by the administration of carminatives, which bring the flatulence away and allow the heart to resume its normal condition. I have had an opportunity of watching a case of severe angina pectoris daily for many weeks, and have been able to satisfy myself that although rise of tension, quick pulse, and cardiac pain usually came on together, yet each might occur separately without the others. A feeling of anxiety often accompanied the pain, but anxiety might occur without pain, and *vice versa*.

Pathology of Angina Pectoris.—The pain is so acute as to resemble neuralgia, and so it has been regarded by some writers as neuralgia of the heart. From observations which I had an opportunity of making in 1867 I came to the conclusion that it was due to spasmodic efforts of the heart to contract against a resistance which was too great for it; that in fact the pain was similar to that felt in the bladder when it is trying in vain to empty itself in face of the resistance of an enlarged prostate. The resemblance is rendered all the more striking by the fact that in both cases when the resistance is removed the pain disappears. It is not mere distension which causes pain in either case for the bladder may become enormously dis-

tended and yet no pain be felt until it tries to contract and empty itself, and great dilatation of either ventricle may occur without pain. Even patients suffering from angina pectoris are, except in very severe cases, free from pain when they are at rest, and it is only when they attempt to make some exertion or are affected by some emotion that pain comes on. Both exertion and emotion raise the blood-pressure, and it is especially after a meal, when they have this power to a greater extent than during fasting, that they bring on pain most easily. An attempt to walk uphill is one of the commonest causes, and if it be made immediately after a full meal the attack may be very severe. In slighter cases the pain ceases when the exertion is stopped, and if exercise is begun very slowly it may not come on at all. If exercise is carefully continued after the first pain is over it may be taken to a very considerable extent without bringing on the pain again. One of my patients expressed to me his great astonishment that although a step or two uphill would bring on the pain, yet after it was over he could walk over his fields as well as many healthy men much younger than himself, shooting partridges.

Angina pectoris is most common in men beyond middle life, in whom tension is higher than normal; but it may occur in men whose tension is normal or even below normal. But just as a weight that would be nothing to a man may be too great for a boy to lift, so a tension below normal may be too great for a weak heart.

In some cases the heart does not seem weak when the patient is quiet, and yet it is unable to meet the least strain. It has no reserve power. I have already mentioned that the heart is very dependent on a free supply of oxygen and becomes weak if this is not fully supplied. In the heart, as in other muscles, this is afforded by a freer supply of oxygenated blood when any work is required of it. But if the coronary arteries be calcified they cannot dilate to supply the necessary blood, and calcification of the coronary arteries is the morbid condition most common in angina pectoris. Whether the same spasmodic contraction which I have described in migraine may occur in the coronary arteries or not is a question regarding which we have no information ; but such contraction, if it existed, would almost certainly cause angina, and the occurrence of vascular spasm in angina abdominis seems to show the possibility of the coronary arteries being stimulated to contraction by a sudden rise in blood-pressure. In some cases there is certainly contraction of the arterioles in the body generally, raising the tension, though observations are not so numerous as one would like, because it is very difficult to make observations in angina pectoris. When the attack comes on, the apparatus for observation is generally not at hand, and even if it is one is so much taken up with trying to relieve the patient that one does not care to trouble him with the application of instruments. In 1866 and 1867 I had an opportunity of making observations in a case of angina pectoris, in

which the attacks occurred every night and lasted two or three hours. During the attack the pulse was very rapid and the arterioles were

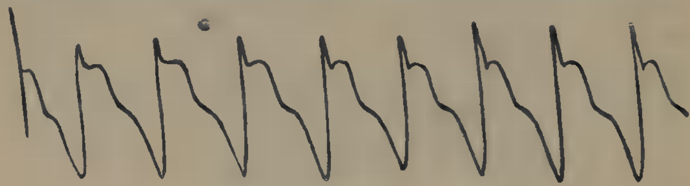


FIG. 60.—Normal pulse.

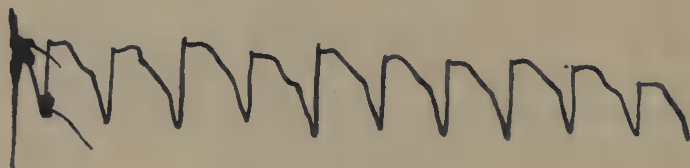


FIG. 61.—During angina.

FIG. 62.—During severe anginal pain.

FIG. 63.—Pain partially relieved by amyl-nitrite.

FIG. 64.—Pain removed by amyl-nitrite.

contracted, as is shown by the very slow fall of the arterial tension during the cardiac diastole. But even with everything at hand I only once succeeded in making an observation, and that

a very imperfect one, of the commencement of an attack, which showed that as the pain came on the tension rose. I was able to make numerous observations regarding the end of an attack, and found that as the tension fell the pain disappeared (Figs. 63 and 67).

Pain very like that of angina may occur in

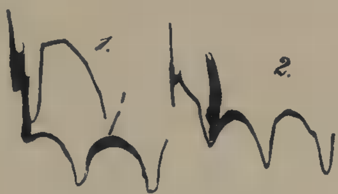


FIG. 65.—Pain coming on at 1; more severe at 2.

FIG. 66.—Anginal attack fully established; pain very severe.

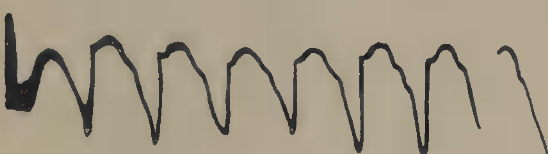


FIG. 67.—Pain relieved by amyl-nitrite.

healthy persons from overstrain in gymnastic exercises, sports, or Alpine climbing, from dyspepsia, or over-smoking. It may also occur in hysteria or Graves's disease. These cases would all be explained by the occurrence of spasm of the coronary vessels such as occurs in migraine.

Claudication and Angina Pectoris. Views of

Allen Burns.—In some old persons whose arteries have become contracted and rigid a peculiar inability for exertion comes on, to which the name of claudication has been given. This condition, which has been observed in animals whose arteries become ossified, was apparently produced experimentally by Allen Burns by means of a moderately tight ligature round the limb, and he recognised the relationship between ossification of the coronary arteries as a danger to life on exertion. He says, "When, therefore, the coronary arteries are ossified every agent capable of increasing the action of the heart, such as exercise, passion, and ardent spirits, must be a source of danger."[22] This view of the pathology of angina pectoris is the one which is now commonly adopted, but it may occur without disease of the coronary arteries.[23]

Views of Sir Benjamin Brodie.—Claudication has been so well described, and its relation to angina pectoris has been so clearly pointed out by Sir Benjamin Brodie in 1846, that I cannot do better than quote his words.

"Such patients," he said, "walk a short distance very well, but when they attempt more than this the muscles seem to be unequal to the task, and they can walk no further. The muscles are not absolutely paralysed, but in a stage approaching to it. The cause of all this is sufficiently obvious. The lower limbs require sometimes a larger and sometimes a smaller supply of blood. During exercise a larger supply is wanted on account of the increased action of the muscles; but, the arteries being ossified or

obliterated, and thus incapable of dilatation, the increased supply cannot be obtained."

"This state of things is not peculiar to the lower limbs. Wherever muscular structures exist, the same cause will produce the same effect. Dr Jenner first, and Dr Parry, of Bath, afterwards, published observations which were supposed to prove that the disease which is usually called 'angina pectoris' depends on ossification of the coronary arteries. . . . When the coronary arteries are in this condition they may be capable of admitting a moderate supply of blood to the muscular structure of the heart; and as long as the patient makes no abnormal exertion, the circulation goes on well enough; when, however, the heart is excited to increased action, whether it be during a fit of passion, or in running, or walking upstairs or lifting weights, then the ossified arteries being incapable of expanding so as to let in the additional quantity of blood which under these circumstances is required, its action stops and syncope ensues; and I say that this exactly corresponds to the sense of weakness and want of muscular power which exists in persons who have the arteries of the legs obstructed or ossified."[24]

Angina Abdominis.—In 1899 I described attacks of abdominal pain under the name of "headache in the stomach," because I thought they were due to spasmodic contraction of the intestinal vessels similar to that in headache (p. 184).[25] Baccelli gave the name of angina abdominis to such attacks, and Huchard of angina pectoris pseudo-gastrique.[26] Pal found

them to be very frequent in tabes, and frequently associated with true angina pectoris.[27] In 1912 Dr Williams and I described a case which resembled angina pectoris in being brought on by exertion and at once relieved by nitroglycerin, exactly in the same way as angina pectoris.[28]

Cardiac Dyspnœa.—The left ventricle supplies the nervous system, the muscles, and the viscera, and, therefore, any interference with its action is indicated more or less by symptoms which may be referred to those structures, such as giddiness, feebleness, or pain like that of angina abdominis already mentioned, or actual pain in the heart itself or in the aorta. The right ventricle supplies the lungs, and interference with its action lessens the respiratory power. For if the blood be kept away from the air, by arrest of the pulmonary circulation, the result is similar to that of keeping the air away from the blood by obstructing the air-passages. I think that cardiac dyspnœa occasionally coincides with angina pectoris, but does not always do so, and great dyspnœa may occur without any actual pain. In some cases, at least, cardiac dyspnœa depends, like angina pectoris, upon partial obliteration of the coronary vessels, and in one case I was able to diagnose atheroma of the coronary artery supplying the right ventricle from the breathlessness of the patient, while the lungs were clear and the left ventricle was strong and active as shown by the forcible apex-beat. The diagnosis might seem to be rather far fetched, but no other was really possible, and

post-mortem examination proved its correctness.[29] In cases of cardiac dyspnœa coming on in sudden attacks the lungs appear to be affected as well, and apparently both the secretion from the pulmonary mucous membrane and the muscular fibre of the bronchioles may be affected, because both dry râles and moist râles are heard in the lungs.

Raynaud's Disease.—Temporary contraction of the arteries and anæmia of the tissues occur in a disease described by Raynaud, and which bears his name.[30] In this disease the arteries contract spasmodically, and I have seen, first of all the tips of the fingers become cold, bloodless, and shrunken like the fingers of a corpse, and this condition gradually extend up the hand in the course of five or ten minutes. Sometimes only one finger is affected, sometimes the whole hand, sometimes the toes, the tips of the ears or the nose, and occasionally, though rarely, the arms and legs. The internal arteries appear also to undergo a similar contraction, especially those of the kidneys and brain, because this disease is frequently associated with hæmoglobinuria and sometimes with epileptic symptoms and transient hemiplegia. The condition is very much like what occurs after immersion of a hand in very cold water, and just as after the hand has been withdrawn it usually becomes swollen, hot, and red, so the extremities after the spasm has passed off in Raynaud's disease become red and hot. On very cold days we notice that even in a healthy person the whiteness of the skin, which indicates both arterial

and venous contraction, is succeeded by arterial contraction with venous dilatation, so that the surface becomes blue instead of white. The same thing occurs in the severer cases of Raynaud's disease, and the term of local asphyxia has been given to the condition. In extremely severe cases the contraction has led to complete stoppage of the blood-supply, and consequent gangrene, like that which occurs in senile degeneration of the vessels.

Chilblains, Urticaria, Angio-neurotic Œdema.—A condition which is very much allied to this, but much milder, is the common one of chilblains. Another ailment which is very troublesome and where there is a local vascular dilatation with effusion of lymph, is urticaria. The wheals characteristic of this complaint are very much like those which are produced by a stinging nettle. They may occur without visible cause, but in some persons with an irritable vascular system they may be produced by simply scratching the skin, so that the patient's name may be written on his back with the finger-nail. In so-called angio-neurotic œdema, instead of mere wheals occurring, the patient may become affected by rapid and intense œdema over a large portion of the body. I have seen in half an hour one side of the patient's face become so much swelled that the left eye was almost closed, and the left side of the face was like that of a patient suffering from advanced renal dropsy, whilst the other side of the face remained perfectly healthy. The pathology of this condition has

not been made out, but the cause of the trouble probably is that there are toxic substances in the blood, for urticarial rashes are very common after the injection of diphtheria antitoxin, and I have seen universal œdema, resembling that of advanced renal dropsy, brought on by the injection of anti-streptococcic serum. The one-sided character of the affection in the case I have just mentioned shows that the nervous system is also deeply concerned in the disease.

Atheroma.—In the arteries, as in the heart, interference with the blood-supply causes degeneration. In one form—the nodular form—there is inflammation in and around the arterial coats with local infiltration about the *vasa vasorum*, leading to spots of degeneration and formation of an atheromatous button, or a patch of nodular arterio-sclerosis. In old people the arterial walls become stiff, and are often as rigid as pipe-stems from calcareous deposit, while the tissue underneath the intima may break up and form rough atheromatous ulcers.[31] One of the most important changes of all is the diffuse arterio-sclerosis, or, as Gull and Sutton call it, arterio-capillary fibrosis, in which the wall becomes thickened from a deposit of hyaline tissue between the muscular and the endothelial coats.[32] This deposit, which is liable to occur in kidney disease, is of great importance, because a lessening of the lumen of the arterioles increases the peripheral resistance, leads to hypertrophy of the heart, and thus to an enormous increase in blood-pressure, with consequent danger of rupture and apoplexy.

High Blood-pressure.—The views of Gull and Sutton were opposed at the time they were put forward by Dr George Johnson,[33] who held that the increased tension was due to contraction of arterioles throughout the body, often accompanied by a hypertrophy of their muscular coat. There appears now to be a considerable amount of evidence that although thickening of the arteries may be one factor in the production of high tension, yet much of it is due to contraction of the arterioles due to stimulation of their muscular coats by toxins. It has now been demonstrated that high arterial tension of itself produces atheromatous changes in the vessels, so that as disease advances both factors may combine to raise the pressure.[34]

Insomnia.—This is sometimes very distressing. In natural sleep the rapidity of circulation in the brain is lessened and its functional activity diminished.* [35] The lessened circulation is probably due to lessened blood-pressure in the brain [36] or from contraction of the carotid arteries and their branches, and if they are rigid and their contractile power be lessened,[37] or if the arterial tension be so high that they cannot sufficiently resist it, sleep is difficult to obtain.

Giddiness.—This is a very common symptom in disordered circulation and is very often associated with faintness. Both symptoms usually indicate imperfect supply of blood to the brain, but they may come on under very

* The dendrons of neurons are amœboid. Ross Harrison, quoted by Mott, *Brit. Med. Journ.*, Sept. 28, 1912, vol. ii., p. 781.

different conditions. In young people they are usually connected with temporary weakness of the heart's action or unusual dilatation of the vessels, causing an abnormally low blood-pressure. In elderly people, on the other hand, giddiness is often an accompaniment of high blood-pressure, but probably its occurrence depends less on the tension than on temporarily impaired blood-supply to the brain from atheroma and contraction of its vessels. It is much more apt to come on if the blood is imperfectly freed from toxins on account of constipation or biliousness. In some patients it is certainly of labyrinthine origin and is frequently accompanied by rushing noises in the ear, synchronous with the pulse and probably depending on atheroma of the arteries of the ear. In such cases a sudden movement of the head may cause so much giddiness as to make the patient fall. A tendency to atheroma which at first only causes giddiness may subsequently affect the coronary arteries and cause angina.

Senile Rise of Pressure.—I must here draw attention to one condition which is very common, and which may become still commoner as increasing medical knowledge regarding the prevention of infective disease leads to prolongation of life. In all men with advancing years the arteries tend to lose their elasticity and become more rigid. The time at which this alteration takes place varies in different individuals and in different families, and the saying is a particularly true one that "a man is as old as his arteries," so that not infrequently we find

strong athletic and robust families who are not only powerful, both physically and mentally, but apparently free from disease, and who are yet short-lived. I believe that these lives might frequently be lengthened by timely attention to the condition of the arteries, more especially by measurement of the blood-pressure, and adjustment of work, of exercise, and of food to the condition that is found. The combination of atheromatous arteries and high blood-pressure is very common, and the risks it entails are twofold: (1) It may lead to cardiac failure, the heart being unable to overcome the excessive tension, and this is all the more common when it is affected by fatty or fibroid degeneration; (2) a vessel may rupture in the brain, and give rise to sudden death, to hemiplegia, or, if the hæmorrhage be small, to local paralysis, sensory affections, or mental deterioration, the result depending on the part of the brain affected. Such small hæmorrhages, according to Ziegler, are very common.[38] Similar results may ensue from blocking of the arteries by atheroma.

Senile Decay.—In the decade for 1891 to 1900 of persons above the age of seventy-five years, no less than 34,822 died from heart disease, and 39,662 from diseases of the blood-vessels.[39] Nor does this even cover all the mischief done by diseases of the blood-vessels, for apoplexy, paralysis, and senile decay may all be reckoned as secondary to disease of the cerebral vessels. In his most instructive book, *On the Nature of Man*, Metch-

nikoff [40] mentions that there are two classes of phagocytes in the body: the small, or microphags; and the large, or macrophags. The

FIG. 68.—Cell from the brain of a woman, aged 100 years, being devoured by macrophags. (From Metchnikoff.)

function of the microphags is to rid us of microbes; that of the macrophags is to heal mechanical injuries, such as hæmorrhages,

FIG. 69.—Section of a renal tubule invaded by macrophags, from the body of an old man, aged 90 years (m=macrophags). (From Metchnikoff.)

wounds, and so forth. In the brains of old persons and animals a number of nerve-cells are surrounded and devoured by macrophags (Fig.

68), and Metchnikoff thinks himself justified in asserting that senile decay is mainly due to the destruction of the higher elements of the organism by macrophags. Other parts of the body also are not safe from their attacks, and the kidneys may likewise suffer (Fig. 69). But the function of the macrophags is not to attack healthy tissues, it is to remove those tissues the vitality of which is destroyed or impaired, and so long as the brain-cells are abundantly supplied with blood they will probably be allowed to remain uninjured by the attacks of the macrophags. I think, therefore, that while senile decay may be actually produced by the macrophags, we are justified in believing that it really originates in an alteration of the blood-vessels.

Embolism and Thrombosis. — When the blood-vessels become obliterated the supply of blood to the parts to which they are distributed may become so insufficient that the tissues die and gangrene ensues, as in old people, where the arterial walls may become so degenerated and their lumen so contracted that the circulation is quite stopped, and senile gangrene of the extremities occurs. Obliteration of an artery may be due to embolism or thrombosis; as, for example, when a clot or vegetation becomes detached from the heart and is carried onwards by the circulation until it is stopped in an artery through which it cannot pass, and which it consequently plugs. Sometimes the arterial wall undergoes atheromatous degeneration, and this may either lead to thrombosis occurring at

the spot where the wall is narrowed, or the atheromatous matter may become dislodged and produce embolism further on ;[41] It is sometimes extremely difficult to diagnose between a case of thrombosis and hæmorrhage ;[42] but if the tension is normal or only slightly raised, the

FIG. 70.—Distribution of the arteries in the brain. (After Ross.)

probabilities are in favour of thrombosis, but if high in favour of hæmorrhage.

If the embolism or thrombosis occur in one of the branches of the Sylvian artery the result may be, as mentioned under *Headache* (p. 186), aphasia, partial blindness, auditory disturbance, or monoplegia ; and if the circulation to the frontal lobe only is affected, there may be mental disturbance without any apparent motor

or sensory symptoms. This will be rendered clearer by a comparison of the distribution of the cerebral arteries (Fig. 70)[43] with that of the cerebral functions (Fig. 71).[44]

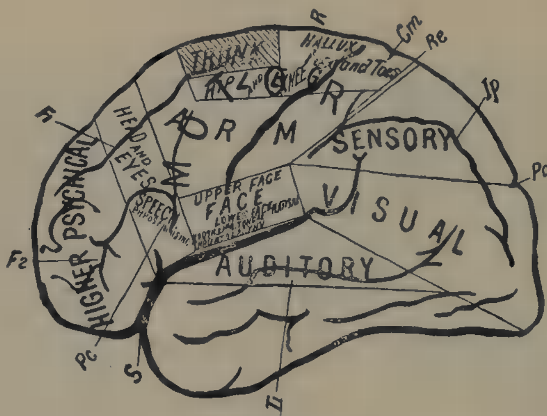


FIG. 71.—Cerebral cortex, showing the distribution of function. (After Osler.)

LITERATURE.

[1] Lauder Brunton, "On Digitalis," etc., *Collected Papers on Circulation and Respiration*, First Series, p. 52 (London: Macmillan & Co.).

[2] Goltz, *Centralbl. f. d. med Wiss.*, 1863, pp. 17, 497; *Arch. f. Path. Anat.*, 1863, vol. xxvi., p. 10 *et seq.*

[3] Goltz, *Centralbl. f. d. med. Wiss.*, 1863, p. 593; and *Arch. f. Path. Anat.*, vol. xxviii., p. 428.

[4] Kratschmer, *Wien. Sitzungsb.*, 1870, Abt. 2, vol. lxvii., p. 24.

[5] Lauder Brunton, *Brit. Med. Journ.*, 4th December 1875, p. 695; and *Practitioner*, 1873, vol. xi., p. 241.

[6] A. Mosso, *Die Diagnostik des Pulses* (Leipzig: Veit & Co., 1879), p. 12; *Arch. Ital. d. Biol.*, 1884, vol. v., p. 130 *et seq.; La Peur*, p. 69 (Paris: Alcan, 1908).

[7] Image, quoted by Lauder Brunton, *Practitioner*, 1873, vol. xi., p. 251.

[8] John Hunter's *Works*, edited by Palmer, 1837, vol. iii., p. 91.

[9] For discussion of low tension, *vide* Janeway, *Clinical Study of Blood Pressure*, p. 152 *et seq.* (New York and London: Appleton, 1904).

[10] von Basch, *Wiener Med. Presse*, No. 8, 1900; *Allg. Physiol. u. Path. d. Kreisl.* p. 74 (Hölder: Vienna, 1892).

[11] Lauder Brunton, *Practitioner*, June 1905, vol. lxxiv., p. 735.

[12] du Bois-Reymond, *Arch. f. Anat. u. Physiol.*, 1860, p. 461 *et seq.*

[13] Lauder Brunton, *Trans. Odontolog. Soc. of Great Britain*, 1880. Reprinted in *Disorders of Digestion*, p. 85 (London: Macmillan).

[14] Lauder Brunton, *Journ. of Mental Science*, April 1902.

[15] Emil du Bois-Reymond, *Arch. f. Anat. u. Physiol.*, etc., 1860, p. 468.

[16] Wm. Russell, *Arterial Hypertonus*, *Sclerosis*, etc., p. 184 (Edin. and London: Green, 1907); E. G. Hawthorne, *Clinical Journ.*, 2nd December 1906.

[17] Goltz, *op. cit.*

[18] Harvey's *Works*, p. 382 (Sydenham Soc., Edin. and London, 1847).

[19] Czermak, *Prager Vierteljahrsch.*, 1868, vol. c., p. 30 *et seq.*

[20] Lauder Brunton, "Cardiac Pain and Angina Pectoris," *Practitioner*, 1891, vol. xlvii., p. 241 *et seq.*

[21] A. Morison, *The Nervous System and Visceral Disease*, p. 757 (Edin. and London: Pentland, 1899); G. A. Gibson, *Diseases of the Heart and Aorta*, pp. 768 and 787 (Edin. and London, 1898); G. A. Gibson, *Nervous Affections of the Heart*, 2nd ed., p. 8 *et seq.* (Edin. and London: Pentland, 1905); Osler, *Angina Pectoris and Allied States* (New York: Appleton, 1897); Mackenzie, *Diseases of the Heart*, etc., p. 42 *et seq.*, 292 *et seq.* (London, 1908).

[22] Allen Burns, *An Inquiry into the Symptoms and Causes of the Syncope Congenosa*, p. 69 (London, 1799).

[23] J. Lindsay Stevens, reprint from *Glasgow Hospital Reports*, 1898, vol. i., p. 236.

[24] Sir Benjamin Brodie, *Lectures on Pathology and Surgery*, p. 360 (London, 1846).

[25] Lauder Brunton, *International Clinics*, 1899, Eighth Series, vol. iii., p. 111 (London : T. Lewin & Co.).

[26] Baccelli, quoted by Minella, *Gaz. d. Ospedali e d. Clin.*, 1902 ; Abstract in *Centralb. f. inn. Med.*, 1903, p. 210. Huchard, *Maladies du Coeur et de l'Aorta*, 3me ed., vol. ii., p. 19, 1899 (Paris : O. Doin).

[27] Pal, *Gefässkrisen* (Leipzig : Hirzel, 1905) ; and *Wien. med. Wochensch.*, 1904, p. 574.

[28] Lauder Brunton and W. E. Williams, *Lancet*, 6th April 1912.

[29] Lauder Brunton, *Practitioner*, June 1905.

[30] Raynaud. For bibliography, see Barlow in Clifford Allbutt's *System of Medicine*, 1899, 1st ed., vol. vi., p. 606.

[31] Ziegler, *Pathologische Anatomie*, 8th ed., p. 54 *et seq.* (Jena : Fischer, 1895).

[32] Gull and Sutton, *Lancet*, 1872, vol. i., p. 794.

[33] Geo. Johnson, *Lancet*, 1877, vol. i., p. 422.

[34] Rickett, *Journ. Path. and Bacteriol.*, 1907, vol. xii., p. 15 *et seq.*, gives experiments and literature.

[35] Durham, *Brit. and For. Med. Chir. Rev.*, 1861, vol. xxvii., pp. 234 and 332 ; R. Jones, *Lancet*, 1913, vol. ii., p. 709.

[36] Friedländer, *Ueber den Isopropylalkohol*, Diss. (Berlin, 1888).

[37] Lauder Brunton, *Brit. Med. Journ.*, 1905, vol. ii., p. 1102 *et seq.*

[38] Ziegler, *Lehrb. d. Pathol. Anat.*, 8th ed., vol. ii., p. 349 (Jena : Fischer, 1895).

[39] Registrar-General in Lauder Brunton on "Longevity," *Lancet*, 17th November 1906, vol. ii., p. 1331.

[40] Metchnikoff, *The Nature of Man*, p. 241, translated by Chalmers Mitchell (London : Heinemann ; New York : Putman, 1903).

[41] For literature of sclerosis and atheroma, *vide* Ziegler,

Lehrb. d. Path. Anat., 8th ed., vol. ii., p. 58, and for arteritis, p. 63 (Jena: Fischer, 1895).

42 Lauder Brunton, *St Bartholomew's Hospital Reports*, 1891, vol. xxvii., p. 225 *et seq.*

43 Ross, *Diseases of the Nervous System*, vol. ii., p. 271, (London: Churchill, 1883).

44 Ferrier, *Functions of the Brain* (London: Smith, Elder & Co.); Mills in Osler's *Practice of Medicine*, 1st ed., p. 890 (Edin.: Pentland, 1892).

CHAPTER IX

ORGANIC DISEASES OF THE HEART

Altered Sounds of the Heart—Alteration in the Second Sound—Accentuation—Gallop Rhythm—Alteration in the First Sound—Cardiac Murmurs—Organic—Functional—Dilatation from Cardiac Strain—Transient Murmurs—Effects of Aortic Stenosis—Effects of Aortic Regurgitation—Failing Compensation—Secondary Incompetence—Effects of Mitral Disease on Cardiac Rhythm—Mitral Regurgitation (organic)—Mitral Obstruction—Cardiac Dyspnœa——Venous Engorgement—Œdema—Albuminuria—Flatulence—Ascites—Effect of Flatulence on Heart—Other Forms of Cardiac Disease—Vicious Circle.

Alteration in the Second Sound. Accentuation.—When we hear a door slammed loudly we know that it is closed quickly in consequence of the application of unusual force; and just as we would expect, when tension is high in the aorta the second sound is louder than usual, or, as it is termed, is accentuated; and this accentuation of the second sound over the aorta is one of great clinical importance, indicating, as it usually does, high arterial tension or aortic atheroma or aneurism. It may be merely temporary and due to physical exertion or emotional excitement. But when it is per-

manent it most commonly indicates arterio-sclerosis or kidney disease. When there is dilatation of the aorta it approaches nearer to the anterior wall of the chest, and the sound is louder than normal. When there is calcification or aneurism of the aorta, the second sound is not merely louder but has a peculiar clanging character. Accentuation over the pulmonary cartilage indicates increased pressure in that artery, such as occurs in mitral stenosis, or regurgitation, or in emphysema.

When a door is closed gently there is little sound. When the pressure in the aortic and pulmonary arteries is low, the second sound is weaker than normal.

Reduplication of the second sound is due to the aortic and pulmonary valves not closing simultaneously, either because the ventricles have not beat simultaneously or because greater relative pressure in the pulmonary artery or aorta has caused prolongation of the systole. It may occur in health from the altered pressure in the pulmonary artery at the end of respiration or beginning of expiration.[1]

Gallop Rhythm.—Normally the diastole is much longer than the interval between the first and second sounds, but if the heart is beating quickly the diastole may become shortened till it equals the interval, and then the sound is like that of a galloping horse.[2]

It may be best imitated by striking with the points of three fingers one after another on the table. It is due to the interpolation of a third sound just at the end of diastole. This is

probably caused by contraction of the auricles. It is of grave significance, and usually indicates great cardiac weakness, occurring in infective disease or chronic renal affections.

Alterations in the First Sound.—The causation of the first sound being more complex, alterations in it occur from a greater number of causes. Reduplication may occur from want of synchronism in the ventricles, but may also arise from an auricular or ventricular additional sound [2] (*cf.* Fig. 15, p. 43). As it is to a great extent a muscular sound,[3] we should naturally expect that weakness of the cardiac muscle, such as occurs in fevers (p. 152), would lessen the sound, and this is exactly what happens. In cases of typhoid fever, when the first sound becomes inaudible, we know that the heart is so weak as to render the prognosis grave. But it would appear that it is not mere muscular strength which causes the sound to become loud, it is rather rapidity of contraction; and even a comparatively feeble heart may have a loud, clear first sound if the tension in the aorta is low, or, in other words, if the resistance it has to overcome is small, so that it can contract rapidly. When the arterial tension is high, and the resistance to be overcome is consequently great, the muscular walls of the ventricle contract comparatively slowly, and even when hypertrophied far beyond their normal size they may give rise to a sound weaker and duller than normal. Of course, the rapid contraction not only gives rise to a greater muscular sound, but it closes the auriculo-ventricular valves

more sharply, and thus increases also the valvular part of the first sound.[4] And yet, again, a heart contracting quickly gives a sharp, or, as it is sometimes called, a slapping impulse to the chest wall, while the more powerful hypertrophied heart, acting on a greater resistance, gives a thudding or pushing impulse not likely to cause so much resonance, and thus the sound will again be diminished. The last factor in the production of the first sound in the heart may also be lessened by a thick layer of lung between the ventricle and the chest wall, as in emphysema, and the lung will also tend to deaden the sound by acting as a non-conductor between the ventricle and the ear. Moreover, the impulse of the heart against the chest wall is also lessened and the sound thus weakened.*

Cardiac Murmurs.—When the aortic valves are destroyed, the sharp "dup" which their closure causes in health disappears, and is replaced by a bruit or murmur.[5] You will most easily understand this by trying to say "dup" with your lips apart, and you will then find that without thinking of it you reproduce the sounds actually heard in aortic incompetency. When it is slight, the closure of the valves is still heard, but is followed by a whiff, as when you say "duff," and in aortic regurgitation the sounds are like "lub-duff." The same happens with the mitral valve, and when this valve alone is incompetent, the sounds of the heart are like

* The Committee of the British Association found the first sound of the heart was louder when the heart struck against a piece of board (*Brit. Ass. Rep.* 1835, p. 246).

"luff-dup," "luff-dup." When both mitral and aortic valves are slightly incompetent, the sounds are like "luff-duff," "luff-duff"; and when both valves are very incompetent, a bellows murmur occurs like "oho-oho."

Cardiac Murmurs. Organic.—The chief cardiac murmurs are those caused by obstruction to the flow of blood onwards through the aortic or mitral orifices or by regurgitation of blood backwards through them in consequence of incompetence of the valves. In the case of the aorta slight roughening of its interior by atheroma may give rise to a systolic murmur, usually heard loudest over the second rib or first intercostal space and propagated toward the neck. This is exceedingly common in elderly people, and may persist for years without the condition causing any symptoms. At the same time it indicates that the aorta is not healthy, and if atheroma should invade the coronary arteries the consequences may be serious. Such a murmur may, however, indicate actual lessening of the aortic orifice (stenosis). Incompetence of the aortic valves is indicated by a diastolic murmur, usually heard loudest over the aortic valves, or rather over the aortic cartilage—propagated down the sternum, and sometimes heard even at the apex. Its presence may sometimes be overlooked, because occasionally it is not heard at the base of the heart at all, but only at the lower end of the sternum, more especially to its left side. Mitral obstruction is indicated by a pre-systolic murmur at the apex which may be imitated by

"hroo-dup." Regurgitation is indicated by a systolic murmur also at the apex.

Both aortic and mitral stenosis are due to contraction of the orifices by inflammatory processes, and aortic and mitral regurgitation are usually due to the valves being damaged by similar processes, leading to deformity and shrinking of the valves, or to the presence of vegetations which prevent the proper apposition of the cusps of the valve.

Functional Murmurs.—But sometimes instead of the valve being too small for the opening, the opening becomes too big for the valve (Fig. 24, p. 75).

Both the aortic and mitral orifices receive support from the muscular fibres which surround them, and when these contract imperfectly the orifice becomes too large for the valves, and regurgitation occurs. Such functional regurgitation is common in the tricuspid and mitral valves, and appears to occur but less commonly in the aortic valves. It was shown by Ludwig and Hesse that when the ventricle contracts normally, the muscular fibres around the auriculo-ventricular orifice lessen it to such an extent that even imperfect valves might close it; but when the heart is dilated, the orifice becomes so large that the valves will not close it, however healthy they may be [6] (Fig. 24, p. 75).

Recent observations of Tait M'Kenzie [7] have shown that murmurs which are almost certainly functional are much more common than has hitherto been believed, and their occurrence

has led to many patients being restricted in their actions when they really required regular physical training. Out of 1000 students 266 were selected who presented no apparent defect to an ordinary test. After exertion by fifty steps taken standing, with the knees high at each step so as to excite the heart, it was again examined, and murmurs were found in 74 out of the 266, that is, 27·8 per cent. In 64 cases it was present at the pulmonary artery, and in 35 per cent at that position only. They were much more frequent in the recumbent position.

The occurrence of cardiac murmurs in nearly 28 per cent of healthy men shows the necessity of not laying too great stress upon their occurrence; but at the same time systolic murmurs at the apex occurring after exertion are apt to indicate that the heart, although in itself healthy, is not strong enough for the amount of exertion that has been employed, so that slight leakage takes place in the mitral valve, and that, therefore, a graduated course of physical training is necessary before any violent exercise is undertaken. In all such cases I think it is advisable to ascertain the effect upon the respiration of some exertion, such as walking quickly or running, so as to gauge the functional capacity of the heart. In his paper Professor Tait M'Kenzie gives an instance of the evil results which may occur from violent exercise undertaken without previous training. I do not know of any good explanation of the pulmonary murmurs which occur in the recumbent position, but it seems just possible that the

pressure upon the pulmonary artery or upon its left branch by the pericardium, dragged downwards and backwards by the weight of the heart, may cause a murmur to originate in the same way as the pressure of the stethoscope upon the sub-clavian artery.

Dilatation from Cardiac Strain.—Such dilatation not only occurs as a sequence to aortic regurgitation, but it also occurs from violent strain in healthy people, or from cardiac weakness. Indeed this happens not infrequently in cases of anæmia and debility, such as occur after acute disease. We then find that a systolic murmur, indicative of mitral regurgitation, becomes very evident, but as the heart gains power the murmur completely disappears. One such murmur I watched with great interest in a girl, who was able to play lawn-tennis without any injury whatever, but every time that she went to a dance the combination of late hours and emotional excitement with active exercise brought on a marked systolic murmur.[8]

Transient Murmurs. — Regurgitation may also occur from irregular action of the musculi papillares, as I observed in some experiments which I made during the year 1865 upon the action of digitalis, and where I heard a mitral regurgitant murmur occur in the heart of a dog which had been poisoned by digitalis, although post-mortem examination showed the heart to be perfectly healthy.[9] Roy and Adami have also made a similar observation with strophanthus.[10]

I have observed a transient mitral murmur

in a patient who tells me he has had it for thirty years. When the heart is quiet there is often no murmur at all, but when its action is excited a loud systolic murmur appears at the apex. It may disappear again in the course of a few minutes. It probably came on originally from severe exertion taken for a wager, when, I think, one of the musculi papillares became strained, so that afterwards it did not always contract synchronously with the others, and thus produced a small chink between the closed valves through which regurgitation took place.

Effects of Aortic Stenosis.—Slight degrees of pure stenosis have little or no effect upon the circulation, but as the work which the ventricle has to do in order to expel the blood is increased by the resistance in front, it usually becomes hypertrophied. As the amount of blood it has to send into the aorta is not more than usual, its cavity does not increase, or, in other words, does not undergo dilatation.

Effects of Aortic Regurgitation. — When there is regurgitation, blood flows back into the ventricle as well as onwards towards the periphery. There is thus a great difference between systolic and diastolic pressure, and the arteries may be seen to pulsate largely. Blood also pours into the ventricle from two orifices, from the auricle and from the aorta, so that the amount of blood it is called upon to hold is greater than usual. Its cavity becomes dilated, and at the same time, in order to send this large wave of blood onwards, its walls require to be stronger than usual. They become thicker, or,

in other words, both dilatation and hypertrophy occur. So long as this compensatory hypertrophy is sufficient to enable the ventricle to do its work, there may be no symptoms at all, and I have seen patients suffering from aortic regurgitation who were nevertheless engaged in arduous physical labour, carrying heavy hods of bricks up ladders many times a day, without knowing that there was anything the matter with them. Not infrequently one may notice that the face has a peculiarly pale waxy look and the arteries show a peculiar irritability (p. 88), so that when the finger-nail is sharply drawn across the forehead a red mark appears which shows three kinds of pulsation.[11]

Failing Compensation. — But the enlarged heart requires an extra supply of blood, and the coronary arteries may by and by become insufficient to supply this, and then cardiac failure commences to set in. When this is the case, symptoms of defective supply of blood to the brain occur, such as indecision, giddiness, tendency to faint, or actual fainting; and symptoms referable to the heart also, such as palpitation, cardiac uneasiness, or anginal pain.

Secondary Incompetence (Functional).—So long as the mitral valves remain competent, the symptoms remain limited to those parts of the body supplied by the aorta. But when the heart dilates so far that the mitral valves no longer close the auriculo-ventricular orifice, so that the blood pours back into the left auricle and pulmonary veins, symptoms of pulmonary engorgement develop (p. 222).

Effect of Mitral Disease on the Cardiac Rhythm.—When the mitral valves become incompetent, the reflux of blood at each beat of a powerful ventricle tends to distend the auricle and the pulmonary veins from which the normal stimulus to ventricular contraction ought to start. In consequence of this the cardiac rhythm is apt to be disturbed, and an irregular pulse will result. For this reason irregularity of the pulse is more frequent in mitral than in any other form of cardiac disease,

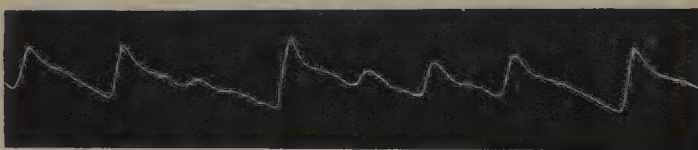


FIG. 72.—Irregular pulse from a case of mitral regurgitation and probably adherent pericardium.

and it is even more marked in mitral obstruction than in mitral regurgitation, probably because in the former disease there is constant instead of intermittent stimulation of the auricle and great veins by the pressure of blood in them.

Mitral Regurgitation (Organic).—Incompetence of the mitral valves occurs from distortion of the valves by inflammation, or by vegetations on their surfaces which prevent them from closing, even more frequently than from dilatation of the auriculo-ventricular orifice. The result, however, is the same. Whenever the valves are incompetent the ventricle drives the blood

at each systole back into the auricle and pulmonary veins, as well as forward into the aorta, and during systole the pressure in the auricle and in the pulmonary veins must be nearly, if not quite so high, as that in the aorta. In consequence of this, the auricle becomes hypertrophied. As there are no valves in the pulmonary veins, it seems extraordinary that the pulmonary vessels do not suffer more than they do, and it appears to me not improbable that the contractile power of the pulmonary veins, which Sir Joseph Fayrer and I rediscovered, may take the strain off the capillaries in the lungs, and thus prevent, to some extent, the tremendous congestion that might otherwise take place.

Mitral Obstruction.—When the mitral valves are much inflamed, they not infrequently become adherent to one another, and the mitral orifice is thus so much narrowed that sometimes it will hardly admit the point of the finger. Great hypertrophy of the auricle then occurs, while the ventricle may be smaller than normal. In such a condition the pressure within the pulmonary veins and the auricle tends to be more or less constantly high, while that in the ventricle becomes low after the systole is over.

I mentioned before, when speaking of the physiology of the heart, that dilatation of the apex of the frog's heart by pressure from within would act as a stimulus to this portion of the ventricle, and cause it to beat rhythmically when it would otherwise remain perfectly still (p. 29). The application of this constant

pressure to the left auricle, while it is absent from the left ventricle, naturally tends to disturb the rhythm, and consequently causes irregularity of the pulse. Moreover, Schiff found[12] that the rhythmical contractions in veins observed by Wharton Jones[13] depend on the pressure inside the veins, being well marked when the pressure is high, and absent when the pressure is low. If this holds good for the venæ cavæ and pulmonary veins, which also possess the power of rhythmical contraction,[14] the pressure of the blood in the pulmonary veins in mitral obstruction may excite stimuli in them, whose rhythm may interfere with others originating in the auricles or ventricles. It is probably in consequence of such abnormal stimuli excited by the pressure in the auricles and pulmonary veins, and possibly in the venæ cavæ, that irregularity of the heart's action is more frequent in mitral constriction than in any other form of cardiac disease.

Cardiac Dyspnœa. — Involuntary muscular fibre seems to have less power of withstanding strain when it is constant than when it is intermittent, and it is in mitral obstruction that we most frequently find the pulmonary capillaries giving way before the strain and hæmoptysis occurring.

Backward pressure in the pulmonary circulation, of course, retards circulation through the lungs; less blood can pass through in a given time, and consequently, both in mitral regurgitation and in mitral obstruction, shortness of breath is a prominent symptom. A patient may

be perfectly comfortable while at rest, but there is no reserve power, and exertion at once brings on quickened breathing and distress, which may sometimes be very severe. In consequence of this obstruction to the pulmonary circulation, the right ventricle has more resistance to overcome; it is obliged to contract with more force, and on account of the increased work tends to become hypertrophied. As a rule, its working power becomes more and more taxed until the maximum is reached, and then it begins to dilate, so that the tricuspid valves become incompetent and the blood pours back into the auricle and the venæ cavæ (*cf.* Fig. 24, p. 75).

Venous Engorgement.—Dilatation and hypertrophy of the auricle occur in the same way as on the left side, but there being no valves in the venæ cavæ, the whole venous system is likely to become engorged. The first indication of venous engorgement is shown in those parts of the body where the venous pressure is greatest, namely, in the feet and ankles, because in these places there is not only the backward pressure which exists in the vena cava itself, but the weight of the column of blood between the feet and the heart. It is this extra weight that determines the yielding of the venous capillaries and the exudation of fluid. This is shown by the fact that when the weight of blood is taken off the feet by keeping them raised upon a high stool or chair during the day, or by putting the patient to bed, the œdema, as a rule, disappears. Next the liver and portal system suffer. The liver becomes congested and enlarged, and

flatulence, both in the stomach and intestine, becomes a troublesome symptom. As the congestion increases the liver may be felt hard, smooth, and large, reaching down sometimes to the iliac crest, pulsation may occur in it, and water exudes into the abdominal cavity, producing ascites. The kidneys also become congested. The increased venous pressure lessens the circulation through the glomeruli, the urine becomes scanty and loaded with lithates, and then albuminuria appears.

Œdema.—The accumulation of serous fluid in the intercellular spaces of the tissues, which constitutes œdema, is due in great measure to venous congestion, but weakness of the vaso-motor nerves also plays a part in its occurrence. By ligaturing the vena cava in a dog, Ranvier caused venous congestion in both extremities, but œdema only came on in the leg of which the sciatic nerve had been cut. He proved that its occurrence was due to paralysis of the vaso-motor, and not of the motor fibres, by cutting the motor roots of the nerve on one side and the sympathetic (vaso-motor) roots on the other. Then œdema came on the side where the sympathetic roots were cut, although the limb retained its motor power, and remained absent from the other limb, although it was paralysed.[15]

Albuminuria. — The albuminuria of venous engorgement is really a kind of œdema in the kidney, the serous fluid flowing away through the ureter just as it does from œdematous legs when they are punctured. It is quite a different thing from albuminuria due to organic disease

of the kidney, and so does not, like it, form a contra-indication to the use of opium. Of course this form of albuminuria may occur in persons who are already suffering from kidney disease, a condition which might necessitate caution.

Flatulence.—The venous stasis in the stomach and intestines prevents the absorption of gas from them, even if it does not increase its formation, and greatly adds to the patient's discomfort.

Ascites. — The usual consequences of abdominal venous congestion are first "wind" and then "water," first intestinal flatulence, and then serous fluid accumulating in the peritoneal cavity, which, by pressing the diaphragm upwards, increases the difficulty of breathing, and by pressing on the ureters obstructs the flow of urine through them and lessens its already too scanty amount.

Effect of Flatulence on the Heart.—Flatulent distension without ascites is very common indeed, and so is flatulent distension with ascites; but ascites without flatulence is rare. The relief which patients with cardiac disturbance feel when flatulence escapes from the stomach is very marked, not only in cases of valvular disease, but in cardiac weakness and in angina pectoris. The *modus operandi* of gastric distension in disturbing the action of the heart is probably twofold. It may depress it reflexly (Fig. 106, p. 358) or mechanically. The heart rests upon the upper surface of the stomach, with only the thin diaphragm between, and if the stomach

is distended it raises the heart up;[16] and by thus altering its position it tends to tilt it up and bring the apex close to the chest wall. It may thus cause palpitation (p. 175). Not only so, but it seems also, by altering the axis, to interfere with the heart's action, and may produce distress or

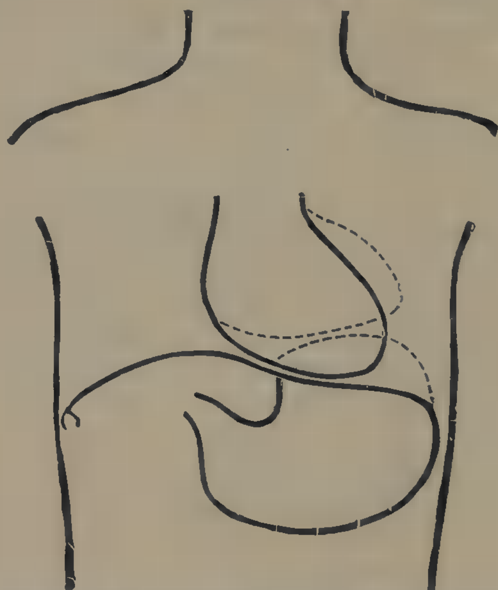


FIG. 73.—Diagram of the effect of flatulent distension of the stomach on the heart. The dark line shows the normal position of the viscera. The dotted line shows their position when the stomach is distended.

even death. Several years ago I saw a notice of a man who died suddenly, and on post-mortem examination he was found to be perfectly healthy, but the stomach was distended with a mixture of potatoes and milk. This had begun to ferment, and the pulpy mass being of an adhesive character, the gas was

unable to escape from it, and caused such distension of the stomach that death occurred.

The mechanism here is, of course, uncertain, because the acute distension may have produced reflex stoppage of the heart, but in all probability the mechanical effect had a great deal to do with it. A year or two ago I saw another similar case recorded, where death was put down to tea. In this instance the bread and tea had apparently formed a mass like the potatoes and milk in the former case, and had a similar effect. In former times one mode of punishing by death was to make the condemned person drink bull's blood warm from the vessels of the slaughtered animal.[17] Blood in itself is not a poison, but as the criminal had to drink it in large quantities it coagulated in the stomach and formed a solid clot which, either reflexly or mechanically, caused death.[18] Under ordinary circumstances distension of the stomach, unless extreme, will not displace the heart and encroach upon the lungs, because the abdominal walls will yield, and the intestines, partially distended as they usually are with gas, will become compressed before any displacement of the heart can occur. But if the abdomen is distended by fluid, or if it is constricted by a belt or by corsets, flatulent pressure, being prevented from exerting its force in a downward or outward direction, will push the heart up, and death may result. For this reason, as was shown by the Hyderabad Chloroform Commission, tight-lacing is dangerous during the administration of anæsthetics.[19] It tends to increase the liability

to palpitation, and explains the efficacy of the common practice of at once loosening the corsets in cases of fainting.

Other forms of Cardiac Disease.—It is obvious that all the conditions I have just described may result as consequences of mitral disease either primary or secondary to aortic regurgitation, but the number of these conditions will be greater or less in other forms of cardiac disease, according to the point in the circulation where the lesion occurs. Thus, we may have all the symptoms of venous engorgement from weakness of the right ventricle and inability to drive the blood through the lungs. This weakness may be absolute, due to fatty degeneration of the cardiac muscle, consequent upon atheroma of the right pulmonary artery; or it may be relative, due to greater resistance to the circulation in the lungs themselves, as, for example, in chronic bronchitis and emphysema. A very instructive experiment in regard to this is that known by the name of Valsalva. If one expires very forcibly against resistance, as by closing both mouth and nostrils, the pulse stops entirely when the pressure reaches a certain point. It is probably from this cause that death sometimes occurs from straining at stool.

In efforts of coughing, expiration is, of course, made against raised pressure caused by the closure of the false vocal cords, which yield in an explosive manner after the pressure has become raised to a certain extent, and mucus is carried out by the forcible stream of air issuing from the lungs. In violent coughing, the effect

of raised pressure in the pulmonary alveoli upon the pulmonary circulation becomes very evident. The face becomes congested, and if the coughing be long continued becomes more or less livid, and the jugular veins stand out largely upon the neck. In people who are otherwise healthy, the ventricle recovers itself when the coughing ceases, but prolonged strain, as in chronic bronchitis or spasmodic asthma, tends to cause permanent dilatation of the right side of the heart, with all its attendant evils.

Vicious Circle.—As in many other things, the conditions in cardiac disease form a vicious circle. The disordered circulation disturbs the functions of other organs, and these in turn make the circulation worse. The condition, indeed, reminds one of the old lines in regard to sorrow :—

> "Sorrow's weight doth heavier grow
> Through debt
> That bankrupt sleep doth sorrow owe."

The disordered circulation interferes with the functions of the lungs, liver, stomach, intestines and kidneys. On account of the difficulty of breathing, exercise becomes impossible, and thus all the accessory aids to circulation given by the muscles and fasciæ during movement are done away with. Appetite becomes lessened and flatulence increases; the elimination of waste products by the kidneys is interfered with, and distension of the abdomen, either by flatulence alone or by flatulence with ascites, presses the diaphragm up, encroaches upon the breathing

space in the lungs, and tilts the heart up, thus still further increasing its difficulties. In such cases it is evident that the patient is bound to die, and to die a somewhat painful death, unless medical art can afford him assistance. It is very fortunate, however, that in such cases medical art can do so much.

LITERATURE.

[1] von Dusch, quoted by Landois and Stirling, *Physiology*, 4th ed., vol. i., p. 83 (London: Griffin, 1891).

[2] For discussion of this, see Gerhardt, *Arch. f. exp. Path. u. Pharm.*, 1894, vol. xxxiv., p. 361; and Sahli, *Lehrb. d. klin. Untersuchungs Methoden*, Leipzig and Vienna, 2nd ed., 1899, p. 276; also, A. James, *Scot. Med. and Surg. Journ.*, June 1899, vol. iv., p. 533.

[3] Ludwig and Dogiel, *Sitzungsb. d. sächs. Gesellsch. d. Wiss. math.-phys. Kl.*, 1868, p. 96; and *Ludwig's Arbeiten* for 1868, p. 75.

[4] Guttmann, *Virch. Arch.*, 1869, vol. xlvi., p. 105 *et seq.*; Ottomar Bayer, *Arch. d. Heilk.*, 1870, vol. xi., p. 157.

[5] *Sixth Report of the British Association*, 1836, p. 264.

[6] Ludwig and Hesse, *Arch. f. Anat. u. Physiol. Anat. Abt.*, 1880, p. 344; Roy and Adami, *Practitioner*, 1890, vol. xliv., p. 348.

[7] Tait-Mackenzie, *Amer. Journ. of Med. Sciences*, 1913, vol. cxliv., p. 69; Schlieps, *Jahrb. f. Kinderheilk.*, September 1912, p. 247.

[8] Lauder Brunton, "Rest and Massage in Cardiac Affections," *Practitioner*, 1893, vol. li., p. 190 *et seq.*

[9] Lauder Brunton, *Collected Papers on Circulation and Respiration*, First Series, 1907, p. 114 (London: Macmillan).

[10] Roy and Adami, *Practitioner*, 1890, vol. xliv., p. 348.

[11] Lauder Brunton, *Journ. of Physiol.*, 1884, vol. 5, p. 14.

[12] Schiff, Roser, and Wunderlichs, *Arch. f. physiol. Heilk.*, 1855, vol. xiii., p. 523.

[13] Wharton Jones, *Phil. Trans.*, 1852, p. 131.
[14] Brunton and Fayrer, *Proc. Roy. Soc.*, 1874, vol. xxii., p. 125 ; and *Proc. Roy. Soc.*, 1876, vol. xxv., p. 72.
[15] Ranvier, *Compt. rend.*, 1869, tome lxix., p. 1326.
[16] Barclay, *Brit. Med. Journ.*, 28th September 1912, p. 778.
[17] Marx, *Giftlehre*, vol. i., p. 268 ; Herodotus, lib. iii., *Thalia*, c. 15.
[18] This explanation was known to Pliny, *Hist. Nat.*, lib. xi., c. 38, section 90, quoted by Marx, *Giftlehre*.
[19] *Med. Press and Circ.*, 1890, vol. i., p. 235 ; *Lancet*, 1890, vol. i., p. 662.

CHAPTER X

METHODS OF TREATMENT IN CARDIAC DISEASE

Uses of Treatment—Rest—Rules regarding Rest for Patients—Position—Commodes—Massage—Results of the combined Use of Rest and Massage—Graduated Exercises—Oxygen—Nauheim Treatment—Baths and Exercises—Oertel's Treatment—Diet—Sports—Milk Diet—Chloride-free Food—Sugar Treatment for Failing Heart—Means of Modifying the Circulation Locally—Heat and Cold—Fomentations—Poultices—Local Bleeding—General Bleeding—Method—Tapping for Œdema—Tapping for Ascites—Plasters over the Heart—Blisters.

Uses of Treatment. **Rest.**—There is perhaps no kind of disease in which the results of treatment are so striking and so encouraging as in cardiac disease. If we can break the vicious circle at one point, we allow recovery to commence; and one of the most important agents—I think I ought to say *the most important agent*—in the physician's power *is absolute rest.*[1] It is very hard indeed to make patients understand what one means by absolute rest. They are inclined sometimes to take the expression as meaning that they shall stay in the house, but that they may go up and down stairs as often

and as quickly as they please. Now, few people have any idea of the amount of work involved in going upstairs. The weight of the body is so evenly distributed upon the muscles of the legs that we hardly feel the exertion in health, but if we suppose that we had fixed upon the bannisters of the stairs on the bedroom floor a strong pulley provided with rope and basket, and that the patient, weighing, let us say, 150 lbs., is put into the basket on the ground floor, and that we had to pull him up by means of the rope, we will then understand the number of foot-pounds involved in the amount of exertion required to bring him from the dining-room floor to his bedroom. The weight is the same and the height is the same when the patient is drawn up in a basket and when he walks up himself. By putting the position before a patient in this way I have sometimes succeeded in convincing him that the work involved in walking upstairs was really great, and more than his enfeebled heart could stand. But it is not merely in walking upstairs that the heart has extra work to do. Even in getting into bed work requires to be done, and, unfortunately, as in the case of a patient whom I saw immediately after giving my third lecture, the exertion of getting into bed may prove fatal.

When patients are well enough to walk gently upstairs, but still require care, they may be instructed to walk upstairs backwards or rather sidewise, as this renders hurry almost impossible.

Rule regarding Rest for Patients. — The advice I give to patients is, that they shall *not*

take one beat out of their heart that can possibly be avoided; that they shall not do one thing for themselves which anybody else can do for them. Nobody else can breathe for them, nobody else can swallow for them, nobody can evacuate for them; but with these exceptions everything else should be done for them. When they wish to sit up in bed, they should be raised up by others; when they wish to turn, others should move them; when they wish to evacuate, a bed-pan should be placed under them.

Position.—But here we are met at once with the great objection that in these severe cases the patient cannot lie down on account of difficulty in breathing. The cause of this difficulty of breathing while in the recumbent position is probably of twofold origin. In the first place, when the patient is supine, the contraction of the diaphragm at each inspiration has to raise the abdominal viscera, while in the upright position it has only to push them horizontally forward.[2] Another cause is probably the extra tension in the right side of the heart, which occurs when the heart is brought down to a level with the splanchnic area; and the comparative ease which occurs in the upright position is due to the blood remaining in the abdomen and limbs, so that the tension in the right side of the heart becomes less. In some cases the facts that when the legs are raised the venous tension in the cava becomes somewhat greater than when they are dependent, and also that when the thighs are swollen there is a little extra pressure exerted on the abdomen,

make it necessary that the patient should be allowed to sit and not be confined to bed. But if he is sitting, he should be kept always in the same position; he should not get up at all, and

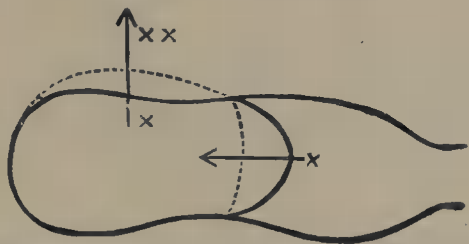


FIG. 74.—Diagram to show the lifting of the abdominal contents during inspiration in the supine position.

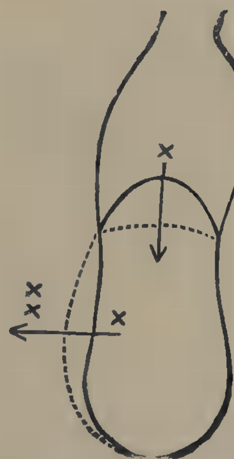


FIG. 75.—Diagram to show the horizontal motion of the abdominal contents in the upright position.

he should have not an ordinary chair but a night-stool, so that the evacuations may be removed without disturbing him. Various beds have been devised upon which patients can lie

comfortably and have their bodies and limbs placed at any angle that is desired without any exertion whatever on the part of the patient; but although these are theoretically very useful, they are not so much used in practice as I think they might be.

Commodes.—One great difficulty in treating many cases of cardiac diseases is that some of them really cannot empty their bowels in the recumbent position. Many say at first that they cannot do it, but with patience and persuasion they learn to do so. In other cases these are in vain and the patients must get up. They must be assisted as much as possible and lifted back into bed, for, as I have said, the exertion of climbing back may prove instantly fatal. It is best to have a commode raised to the height of the bed on some kind of platform so that the patient can simply be shoved on and off it without altering the level of his pelvis, the only change being in the relative position of the trunk and limbs. Commodes are now made which effect this purpose.[3]

Use of Massage.—It is evident that when the patient is resting completely, either in bed or in a chair, all the accessory means of circulation in the limbs of which I have already spoken are absent, and not infrequently one finds that the feeble circulation in the muscles, and the consequent accumulation of waste products, give rise to feelings of heaviness in the limbs, discomfort, and restlessness which are very trying to the patient. In health, the arteries which run in the same sheath as the nerves exercise a

kind of massage upon them by their alternate contraction and expansion, in the same way as on the veins; but when the pulse is feeble the nerves suffer in consequence.* The indication for treatment here is to replace the natural accessories to circulation as far as possible by artificial ones, and this we are able to do to a certain extent by skilful massage. Massage is one of the most powerful agents in the treatment of such cases.[4] It is a therapeutic agent of very great power and value; but, like opium, which from its utility has been termed God's greatest gift to man, it is liable to abuse, and on account of its abuse it is often looked upon askance. But just as we cannot afford to throw opium aside as a medicine because it is liable to abuse, so we must employ massage if we are to do the best for our patients, and at the same time we must guard as far as possible against any chance of abuse. By slow, firm, upward strokes along the legs and arms, the venous blood is forced onwards towards the heart, and the fluid which has accumulated in the intercellular tissue is drawn on into the lymphatics. Thus the resistance which the flow of blood through the arterioles and capillaries has to overcome is lessened, and the work of the heart lightened. The weariness, the weight, and the discomfort of the limbs are removed, and the restlessness and irritability of the patient lessened. Over-massage, however, acts like over-exercise, and does harm.

Results of Combined Rest and Massage.—The combined effects of rest and massage are

* *Vide* p. 156.

that the heart beats more slowly, has a longer period of repose between each beat, and has less work to do at each systole. Thus the process of repair is allowed to begin.

The lessened resistance allows each cavity to contract more perfectly, the longer pause allows each cavity to become more full of blood, the larger pulse-wave sent into the vessels at each ventricular contraction increases the amplitude of the pulse in the arteries, and thus brings about a more efficient self-massage in the arterial walls, and consequently a more efficient return of blood and lymph from the veins and lymphatics, which accompany the arteries in their sheaths.

The heart itself, by means of its more efficient self-massage, gets rid of its waste products, is better supplied with blood, and gradually becomes stronger and stronger, until finally many patients who seemed moribund recover under the influence of rest and massage to such an extent that they may become practically well and remain so for years.

But it is not only on the heart and vessels that the influence of rest and massage and the consequent improvement of the circulation is noticed. On account of the increased circulation through the muscles waste products are more thoroughly oxidised, and, the massage taking the place of exercise, a better appetite for food is produced, whilst the diminished congestion of the liver, stomach, and intestines improves digestion, and thus lessens flatulence. Massage to the abdomen aids this process; it

tends to cause expulsion of gas from the stomach and intestines, and thus decreases the mechanical interference which the abdominal distension exerts upon the lungs and heart. The freer circulation tells upon the kidneys also. The urine becomes more abundant in quantity, albumen disappears, waste is more freely eliminated, and absorption goes on both from the inter-cellular tissue and serous cavities, so that the œdema of the limbs and fluid accumulated in the peritoneal or pleural cavities become absorbed, and the œdema, ascites, or pleural effusion disappears. Pleural effusion is, of course, a very serious complication in valvular disease, encroaching, as it does, upon the available breathing space, and its appearance should always be carefully watched for, more especially as its occurrence is often insidious. It is, however, less common and less disturbing than abdominal distention by gas or water, or both.

Graduated Exercises.—For patients who are so ill as to be confined to bed gentle movements may be useful, and may be employed along with massage. They should be increased very gradually. For example, the patient may bend one finger gently against resistance the first day or even the first forenoon. In the afternoon he may straighten the same finger against resistance. Next day he may bend two fingers, and in the afternoon extend two fingers, and so on, gradually including the wrist, the fore-arm, and even the arm. The resistance should at first be very slight indeed, and may be gradually

increased as the patient can bear it. Such gentle movement as simply flexing a finger might seem at first sight to be useless, but if anyone will put his hand upon his biceps and get someone else to hold his finger while he flexes against resistance, he will soon discover that it is not merely the muscles of the finger alone that are in action, but that the biceps, and even the muscles of the trunk take part in the move-

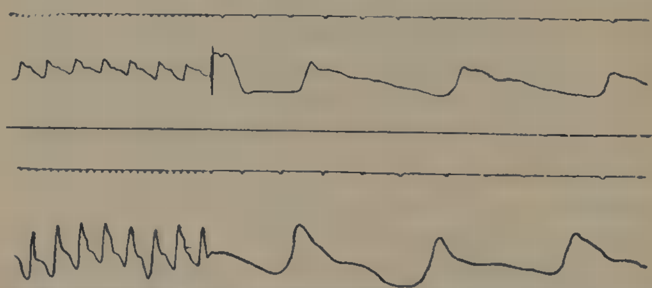


FIG. 76.—Pulse tracing, showing the effect of massage and graduated movements. Each tracing is taken partly with a slow and partly with a quick movement of the sphygmograph. The upper shows high tension and a feeble heart; the lower shows less tension and a stronger heart. The tracings I owe to the kindness of Dr Gustav Hamel, to whose treatment I had recommended the patient.

ment. The effect of massage and exercises on the pulse is shown by the tracing above (Fig. 76), where the high tension with slight movement of the radial artery is converted into less tension, quicker contraction of the heart, and more active movement of the vessel, increasing the self-massage both of the arteries and the heart.

Oxygen. — Inhalation of oxygen certainly gives great help in severe cases, and I think it is possible that occasionally the deep inhalations

which patients take when they are inhaling the oxygen may help mechanically by producing self-massage of the heart. They also lessen the viscosity of the blood, and thus aid the circulation. A mask is usually supplied to fit over the patient's face, but many patients dislike this and prefer a tube simply placed in the mouth,[5] or a funnel held before the nose.

I do not think it is possible to give too much oxygen. In some cases I have given it for more than a week continuously with the best results. For this purpose it is best to hang a funnel at a short distance above the patient's nose and mouth so that the oxygen may stream constantly down on them.

It is not infrequently desirable to administer nitrite of amyl, or iodide of ethyl, along with oxygen to patients suffering from anginal attacks or spasmodic asthma. This may be done by putting the medicament upon a piece of blotting-paper or cotton-wool in the funnel or inhaler close to the patient's face. The inconvenience of this is that the apparatus is apt to move from its position, and there is no means of regulating the strength of the inhalation. To obviate these inconveniences a bottle has been made for me by Messrs Allen & Hanburys, with two metal tubes arranged similarly to those of an ordinary Woulfe's bottle (Fig. 77). One of these, however, can be moved up and down, and may be fastened by means of a screw, as shown in the illustration. The cotton-wool or blotting-paper, moistened with nitrite or iodide, is placed in the bottle. At first the movable tube is drawn well

up, so that as the oxygen passes through it over the wool the vapour is dilute. As the nitrite evaporates the tube is pushed further down so as to go closer to the paper or wool, and thus a stronger vapour is obtained. When it is desired to give a diffusible stimulant, ether may be

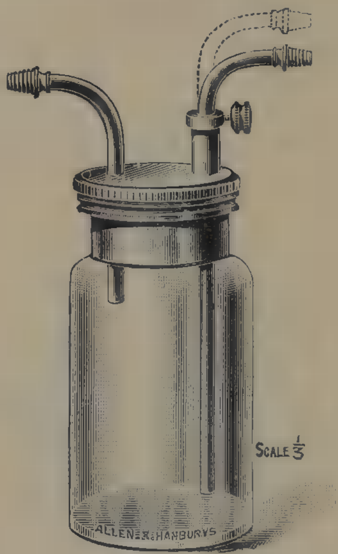


FIG. 77.—Bottle for medicating oxygen.

employed in a similar way, or a quantity of rectified spirit, brandy, or whisky may be poured into the lower part of the flask and oxygen allowed to bubble through it. The bottle may also be used simply to render the oxygen warm and moist. In this latter case the bottle is half filled with hot water and placed in a small basin of hot water, or surrounded by hot wet flannels.

In some cases of bronchitis it may be advisable to add to the hot water Friar's balsam, terebene, or other terebinthine preparation.[6]

In very bad cases artificial respiration may be performed with oxygen.[7] The instrument for this purpose is shown in Fig. 78. It consists of a stopcock of peculiar construction which is connected by an india-rubber tube at one end to a cylinder containing oxygen, and at the other terminates in two nozzles which pass

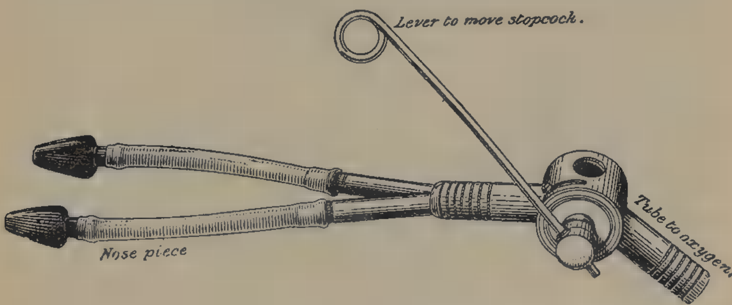


FIG. 78.—Stopcock for artificial respiration with oxygen.

into the nostrils. By moving a short lever the nostrils are alternately put into communication with the oxygen cylinder and with the open air, so that, by moving the lever alternately backwards, and forwards, artificial respiration is kept up with the minimum of exertion, so that it may be continued if necessary for hours.

Nauheim Treatment.—For cases of weak heart and tendency to venous engorgement the treatment by baths and exercises is also useful. The system of applying them has been well worked out by the brothers Augustus and

Theodore Schott, at Nauheim, and the treatment is often known now as the "Nauheim" treatment.[8] At Nauheim the water as it issues from the springs is very highly charged with carbonic acid, but this is allowed to escape, and the water to become still, for the baths which are given at first, and it is only in the later baths that the effervescent water is employed.

Baths.—Baths are usually employed daily for three days, then omitted for one day, during a course of three to six weeks, or even longer, according to the condition of the patient. The bath at first lasts only about six minutes, at a temperature of 95°. The duration is then increased to eight or ten minutes, and the temperature is lowered to 92°. They are then strengthened further with the mother liquor obtained by evaporating the ordinary water. The duration is gradually increased to fifteen or twenty minutes and the temperature lowered as far as 82°. Immediately after the bath the patient is rubbed dry with hot sheets by an attendant, and then must rest for at least an hour. The effect of the baths is generally somewhat to slow the pulse. This effect on the pulse-rate is not so marked as that on its quality, for they render it much fuller and softer (see Figs. 79-84, pp. 246-7).

On alternate days movements may be used, or daily, according to the patient's condition. I give here a list of the movements, which Professor Schott at Nauheim kindly got his attendant to show me. Six to twelve of these movements may be given at a time, and they

should be selected so that alternate movements shall affect different sets of muscles.

Exercises.—The essential part of these movements is that the movement shall be slow and regular, and that each movement shall be fully carried out. The body should be held upright, the joints should be kept straight, and the resistance applied should not be sufficiently great to cause any tremor of the limbs or shortness of breath in the patient. The resistance may either be applied by the patient himself putting into action the opposing muscles to those which effect the movement, or by an attendant or friend gently opposing the movements.

I. The arms are to be raised slowly outwards from the side until they are on a level with the shoulder. After a pause they should be slowly lowered.

II. The body should be inclined sideways as much as possible towards the right, and then to the left.

III. One leg should be extended as far as possible sideways from the body, the patient steadying himself by holding on to a chair. The leg is then dropped back. The same movements are repeated by the other leg.

IV. The arms are raised in front of the body to a level with the shoulder, and then put down.

V. The hands are rested on the hips, and the body is bent forwards as far as possible, and then raised to the upright position.

VI. One leg is raised with the knee straight forwards as far as possible, then brought back. This movement is repeated with the other leg.

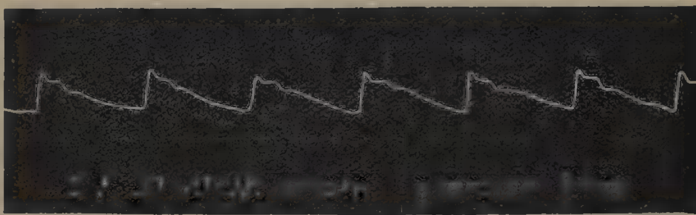


FIG. 79.—Tracing from the pulse of a patient, aged 62, with a gouty kidney and failing heart. This tracing and the five following from the same patient show the effect on the pulse of exercises and baths.

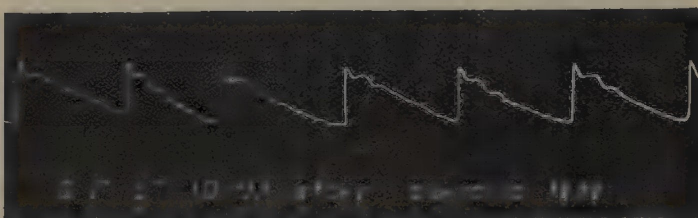


FIG. 80.—Effect of exercise.

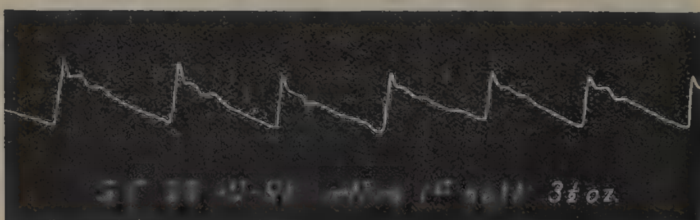


FIG. 81.—Before first bath.

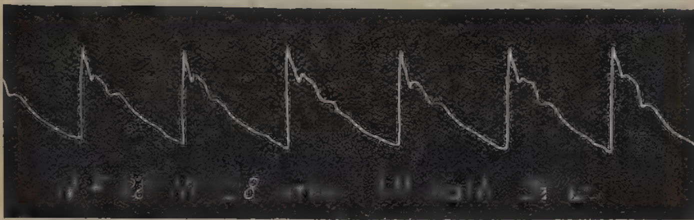


FIG. 82.—Effect of one bath.

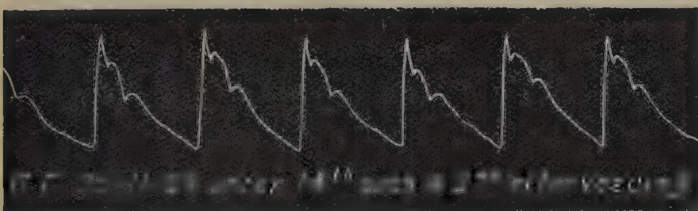


FIG. 83.—Effect of saline and effervescing baths.

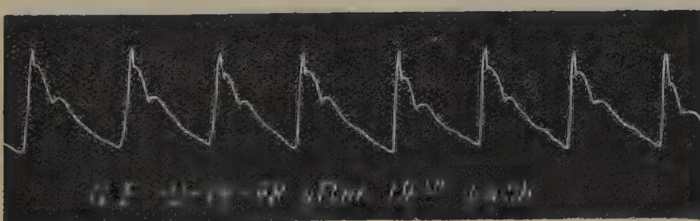


FIG. 84.—Effect of nineteen baths.

VII. With the hands on the hips, the body is twisted round as far as possible to the right, and then again to the left.

VIII. With the hands resting on a chair and the back stiff and straight, each leg is raised as far as possible backwards, first one and then the other.

IX. The arms are extended and the fists supinated. The arms are then moved first outwards, next inwards at the height of the body.

X. Each knee is first raised as far as possible to the body, and then the leg extended.

XI. This movement is the same as IX., but with the fists pronated.

XII. Each leg is bent backwards from the knee and then straightened.

XIII. Each arm is bent and straightened from the elbow.

XIV. The arms are brought from the sides forwards and upwards, then downwards and back as far as they will go, the elbows and the hands being straight.

XV. The arms are put at a level with the shoulder, and then bent from the elbow inwards and again extended.

XVI. With the arms in front at the level of the shoulder and the hands stretched, the arms are opened out sideways and then brought together.

XVII. The arms are bent from the elbow outwards and extended.

There should be a pause of half a minute between each successive movement, such as raising the arms and lowering them, and a

pause of one or two minutes between the movements of different kinds, such as I. and II.

Personal Observations on the Nauheim Treatment.—The results of observations made upon myself during a mild course of five weeks at Nauheim under the care of Professor Schott were:—

The pulse-rate was little affected either by baths, massage, or movements, but each of these means of cure altered its character, rendering it fuller and softer.

The blood-pressure was little affected either by baths or massage, but was almost invariably lowered 5 mm. by exercises.

The result in five weeks was increase of strength, greater ability for exercise, diminished dilatation of the heart, as ascertained by percussion and reduction of the blood-pressure to the normal.[9]

After-Cure.—After the course is over it is advisable for the patient to go to some place for an after-cure, where he can follow up the treatment by graduated exercise.

The best after-cure consists in daily walks in which both the distance travelled and the steepness of the road are very gradually increased, great care being taken not to cause exhaustion or strain, which might undo all the good obtained from the cure. Walks are laid out for this purpose very carefully at Badenweiler, in Germany; but there are a great number of places both at home and abroad where suitable conditions can be found with walks on

the flat and more or less steeply inclined along a hillside. In Switzerland especially there are numerous places of this sort, and the fresh air there seems to have an invigorating action. Many people with cardiac disease cannot go without discomfort to a height exceeding 2000 feet, while others feel better at greater elevations, though the number of those who care to go as high as 7000 feet is small, and if the arterial tension is high such altitudes should be avoided.

Oertel's Treatment. — This treatment by graduated exercise is often known as Oertel's. The principles upon which it depends are—(1) That the cardiac symptoms are due to disproportion between the force of the heart and the resistance it has to overcome; and (2) this disproportion is to be remedied by dietetics and by exercise, consisting chiefly of graduated walking uphill.[10]

The dietetic rules are—(1) Give such food as will strengthen the cardiac muscle; and (2) diminish the amount of liquid consumed, in order to reduce the mass of circulating blood.

The exercises are intended to promote elimination of liquid, especially through the lungs and skin, and to increase the nutrition and activity of the heart. In aortic regurgitation, Dr Schott considers that the work of the heart is easier when there is abundance of blood to make up for the loss in the general circulation sustained by regurgitation during the diastole. He, therefore, advises a very full diet; but in mitral disease, where the patient,

on account of breathlessness, can move less than a healthy person, he advises a sparing diet. In chronic myocarditis, where albumen is required, but not nuclein, butcher's meat should be given sparingly, but milk and plasmon freely. In aortic disease he allows two pints of fluid a day, and as much as three pints if the weather be hot; but if there is any interference with the pulmonary circulation, as shown by shortness of breath, he only allows between a pint and a half and two pints. In mitral disease he only allows about a pint and a quarter to a pint and a half.

The exercise consists in gentle walking up graduated slopes. The first walk is taken upon a very gentle slope, and only for a short distance. This is increased daily, and when the patient can walk on the level or gentle slope without shortness of breath, he walks up a somewhat steeper grade. The steepness of the ascent and the lengths of the walks are gradually increased as the patient's heart will bear it.[11]

Exercise. Games. Sports.—The questions are constantly asked by patients suffering from cardiac disease: "What exercise may I take? May I play tennis or golf? May I cycle, fish, shoot, ride or hunt?" The answers to these questions differ not only according to the nature and extent of the cardiac disease, but according to the patient's temperament and disposition; for while one patient will do exactly as he is told, another will be timorous and do too little, while a third will interpret any liberty that is allowed him in the very widest sense, and make

efforts that are not only foolish but dangerous to his life. The great rule is to take as much exercise as possible without causing strain or bringing on much fatigue. When fatigue comes on, the exercise should stop. If his exercise should take the patient away from home, he must always remember that he has to get back, whether he be walking, riding, or cycling, and must turn back in good time so that he shall not be obliged to continue the exercise after he begins to feel tired. All severe sudden strains should be avoided, such as riding a bicycle up hill or in face of a wind, riding a restless horse, taking a big jump in hunting or playing lawn-tennis, cricket, or golf in a match where the player feels that he must do the best he can for his side regardless of the consequences. The same is the case in rowing. Paddling in a small boat is sometimes very good for slight cardiac cases, for it gives amusement and just enough exercise to benefit the circulation without causing strain. For people who require exercise and have very little time to take it, a rowing machine is good because the resistance, rate of movement, and duration of the exercise can be accurately adjusted.

Milk Diet and Chloride-free Food.—Lately a great deal of attention has been given, especially in France, to the effect of chlorides upon transudation from the vessels into the tissues.[12] Chlorides appear to favour this, and therefore, although they may be useful in health, they are disadvantageous in dropsy, and accordingly a diet containing only a small quantity of chlorides is used. Calcium and

its salts appear to have a contrary action, and rather to diminish transudation. The amount of chlorides in milk is not great, the quantity of calcium is considerable,[13] and the lactose appears to have a diuretic action;[14] so that frequently we notice patients suffering from mitral disease when put to bed with entire rest, with massage, with an entirely milk diet, just as if they were typhoid patients, and with a pill of digitalis, blue pill and squill, frequently improve with great rapidity. But a milk diet does not always suit; and consequently bread made with sugar instead of salt, farinaceous preparations also made with sugar and without salt, and boiled meat without salt, but with sweetened tomato sauce or some such condiment to make it pleasant, and eggs, either boiled without salt or in the form of a sweet omelette, and plasmon, may all be used. I have only tried this in a few cases, but certainly the treatment has appeared satisfactory.

Sugar Treatment of Failing Heart.—The nutritive power of sugar has been utilised in cases of cardiac weakness by Dr Goulston[15] and by Dr Carter[16] (*vide* p. 287).

Local Modification of the Circulation. Heat and Cold.—We have various methods of modifying the circulation locally. In local inflammations, aconite seems to be useful, and during its administration the local inflammation frequently subsides, the pain disappearing, the redness, swelling, and heat of the part diminishing. We may modify the local circulation in inflammation either by heat

or cold. If the inflammation be situated in a place where the tissues are yielding, heat frequently relieves it most; but if the tissues are unyielding, as, for example, where the inflammation occurs at the root of a tooth or under a hard fascia, heat increases the pain, while cold relieves it. The explanation of this is obvious. Heat tends to cause local dilation of the vessels, and if the nerves which run alongside them are in an unyielding sheath, the dilated vessels press more upon them and increase the pain; whereas if the tissues are yielding all round, the collateral circulation is increased, and the pressure of blood in the inflamed area is lessened. If the nerves and vessels are both confined in an unyielding sheath, the application of cold tends to cause contraction of the vessels, and, by diminishing their calibre, to lessen pressure upon the nerves and ease the pain. The local application of heat may induce a pretty extensive dilatation of the vessels; for, on putting my feet into a bath of hot water, I have sometimes observed increased pulsation of the femoral arteries. The local application of cold in the case of an artery will cause it to contract, and lessen the circulation in the distal part; so that if a cold bandage be applied over the middle of the arm, the radial artery will beat less strongly.[17] By putting on a cold bandage covered with oil-silk a gentle warmth of the surface is produced, which seems to have a quieting effect upon the circulation, and lessens the pain from inflammation, as is evident from its use in various local lesions, and

perhaps most markedly when applied to the throat in cases of pharyngitis and tonsillitis. A large wet compress of this sort applied to the abdomen is sometimes very useful in cases of sleeplessness, as it tends to draw away the blood from the brain and allow the nerve cells to become quiet. Warmth to the inside of the stomach has a similar action, and warm food will often tend to produce sleep. The food must, however, not be too warm, as otherwise the heat will pass through the diaphragm, and by its local stimulating action on the heart will increase the force of the pulse, and by driving more blood to the brain, lessen the tendency to sleep instead of increasing it.

Poultices.—These applications often give the greatest possible relief in pain due to pleurisy or pericarditis, as well as to pains of a colicky nature. They are usually made of crushed linseed, bread-crumb, arrowroot, or oatmeal, and some mustard flour is often added to them. They are frequently applied to the skin with nothing between them and it except perhaps a layer of muslin. In the case of poultices of mustard flour alone or of poultices in which its irritant action is desired, this is quite right, and also where linseed poultices are used for their local soothing and demulcent action on wounds or ulcers. But this method is not the best where poultices are required to soothe pain inside the thorax or abdomen.[18] For if we apply the poultice directly to the skin we either burn it and cause great pain to the patient, or we must wait until it is cool enough

to be borne, and then much of its warmth is lost. But if two layers of flannel be interposed between the poultice and the skin it may be put on as hot as it can possibly be made.

A convenient way of making a poultice is to prepare a flannel bag about twelve inches by eight; this should be closed at three edges and open at the fourth; one side of it should be about one inch or one inch and a half longer than the other, and it is convenient also to have four tapes attached at the points which form the corners when the bag is closed, in order to keep the poultice in position. Besides this, another strip of flannel should be prepared of the same breadth as the length of the bag, and long enough to wrap round it once or oftener. Crushed linseed, bowl, and spoon should then be got together, and the spoon and bowl thoroughly heated by means of boiling water; the poultice should then be made with perfectly boiling water, and rather soft. As soon as it is ready, it should be poured into the bag, previously warmed by holding it before the fire; the flap which is formed by the longest side of the bag should now be turned down and fastened in its place by a few long stitches with a needle and thread; it should then be quickly wrapped in the strip of flannel (also previously warmed), and fastened *in situ*, if necessary, by means of the tapes. It may be covered outside with a sheet of cotton wool. In this way the poultice may be applied boiling hot to the skin without burning; the two layers of flannel which are at first dry allow the heat to pass

very gradually indeed to the skin; as the moisture of the poultice soaks through them, they become better conductors, and the heat passes more quickly, but the increase is so gradual as not to cause any painful sensations whatever, but only one of soothing and comfort. The poultice also naturally keeps much longer hot, and the necessity for changing it arises much less frequently.

An india-rubber bag laid over one or two layers of moist flannel is sometimes a convenient substitute for a poultice.

Hot Air Bath.—By placing an arm or leg in a hot air bath at 240° F. the temperature of the whole body may be raised and cardiac pain sometimes diminished. Of course the limb must be carefully protected by cotton wool or by some other material which does not conduct heat easily, so as to protect it from being burned.[19]

Local Bleeding.—A means of influencing the circulation locally, which was formerly much employed, but has now to a great extent fallen into disuse, is the application of leeches and cupping. The relief which is obtained by the application of half a dozen leeches to the side, in cases of severe pleurisy, is very extraordinary; and it is difficult indeed to see how the comparatively small quantity of blood which they extract should relieve the patient so much; but there can be no doubt about the fact that the relief they afford is enormous. Their application over the mastoid process in severe headache or in meningitis, and over

the cardiac area in pericarditis or the liver in hepatitis, especially if accompanied with perihepatitis, is very useful. Wet cupping over the kidneys in acute nephritis, and over the back in suffocative bronchitis, is sometimes attended with marked amelioration of the symptoms. It is not simply the removal of blood that produces this effect, because dry cupping, where no blood is removed, is frequently of service. In dry cupping the beneficial result may be partly due to the withdrawal of blood to the skin and subcutaneous tissue. It may also be due to a reflex effect of the stimulus upon the circulation, both local and general, and it may possibly be, to some extent, a form of serum therapeutics, as the fluid which exudes into the tissues after the application of the cups may undergo some alteration which imparts to it a curative action after its reabsorption. Any explanation of the mode of action, however, is at present hypothetical, and we are obliged to be content with knowing what the effects are without understanding how they are produced.

General Bleeding.—Bleeding from the arm is a remedy which is now too little used. In the case of angina pectoris, in which I used nitrite of amyl for the first time, small bleedings of three or four ounces were the only thing which eased the pain before the nitrate was employed, and even after its employment bleeding from the arm benefited the patient. In engorged conditions of the

right side of the heart, whether due to mitral incompetence or pulmonary affections, blood-letting not only relieves the symptoms, but may save the patient's life.

Method of Bleeding.—Bleeding used at one time to be practised by barbers and black-smiths, and was so much in fashion that it was often used every spring as a matter of routine whether the person bled was ill or not. Its abuse led to its disuse, and now it is so little used that many men in practice have never bled a patient and hardly know how to do it or what instrument to use. In my opinion it should not be done with a bistoury, but with an old-fashioned lancet, which is much better. A bandage is put tightly round the upper arm so as to prevent the return of venous blood and a tight roll of paper, a stick, or something similar put into the patient's hand so that he may alternately grasp it firmly and loosely, and by the motion of his muscles drive the blood into the veins. The striped pole which is still used as a sign by barbers represents the stick which they used in bleeding and the stripes round it represent the bandage. When the veins stand out well a slight cut is made with the lancet into either the median cephalic or median basilic, care being taken that the cut skin does not become displaced, for the cut in it and in the vein must coincide.

As the blood spurts from the distended vein a vessel must be held in such a manner as to catch it, for otherwise both clothes and bed-clothes may be much soiled.

If blood refuses to flow, as it does when patients are too far gone, the forearm may be squeezed and rubbed in an upward direction, and oxygen given to aerate the blood (*vide* p. 240).

Usually the abstraction of ten or fifteen ounces is sufficient at a time, for it is not the mere quantity abstracted that does the good.

In cases of very high tension I believe that the repeated abstraction of small quantities of blood from time to time may do much good, and in my paper on the use of nitrite of amyl in angina pectoris in the *Lancet* for 27th July 1867, I recommended that in severe cases of this disease, in addition to the use of nitrite of amyl in a paroxysm, bleeding should be performed about every fortnight.[20] Such frequent bleedings as this, though they were the only means of relieving my patient before I used the nitrite, are probably unnecessary in most cases now, as we now know other means of reducing tension.

Tapping for Œdema.—The simplest way of tapping the legs for œdema is simply to run an ordinary sewing needle into them in a number of places and then cover them with absorbent cotton-wool, which absorbs the serum as it exudes. The legs should be previously washed with some disinfecting solution and the needle also rendered aseptic. Some prefer a triangular to a sewing needle, and sometimes fine cannulæ introduced by a trocar and fitted with a long india-rubber tube to carry off the fluid are preferable to either.

Tapping for Ascites.—This is often delayed unduly by the patient's fear of it, but this may often be overcome by using a very small trocar and cannula from $\frac{1}{16}$th to $\frac{1}{8}$th of an inch in internal diameter. Before introducing this, three or four feet of fine rubber tubing should be tied to the outer end of the cannula, and pulled down over the opening. The trocar is then pushed through the rubber into the cannula. Before this is done the cannula and tubing may be filled with disinfecting solution, *e.g.*, of carbolic acid 1 in 20, and the tubing tied in a knot at its lower end to prevent the fluid escaping. The skin is then disinfected, and if the patient is very sensitive it may be anæsthised by ether spray, cocaine or novocaine. The trocar is then pushed through the abdominal parietes, the knot in the tubing undone and the trocar withdrawn. The elasticity of the rubber closes up the hole made in it by the trocar and no fluid comes through it, but the carbolic solution at once begins to flow into a pail or basin on the floor, in which some of the same solution may also be placed. On account of the small diameter of the tube the fluid flows out slowly, and this has the advantage of lessening any chance of syncope. If the medical attendant had to stay a long time it would have the grave disadvantage of interfering seriously with his other work. But this is unnecessary, for if the tube is properly fastened to the abdominal wall it may be left for a couple of hours without injury to the patient and even without his being conscious of its presence. The best way of doing this is by strips of adhesive

plaster with two cuts in each piece so that its middle can be raised and the tubing passed under it. The strip is then fixed to the abdominal wall and keeps the tubing perfectly in position. If necessary more than one strip may be used (Fig. 85).

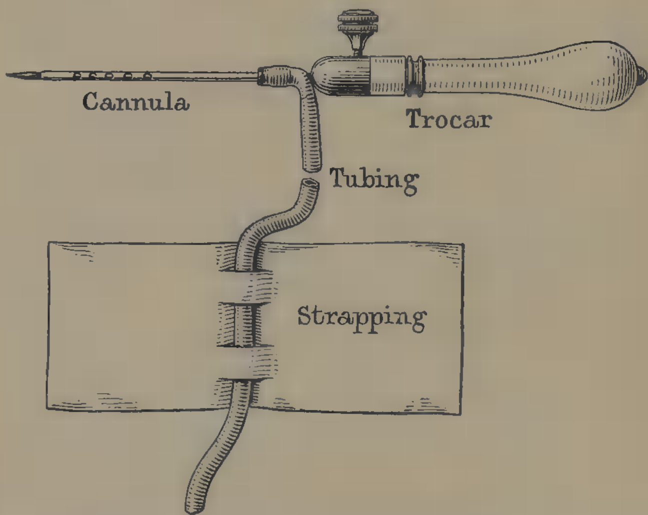


FIG. 85.—Diagram of the method of tapping in ascites and fixing the tubing described in the text.

Plasters over the Heart.—These probably act reflexly, but we do not know. There can be little or no doubt, however, of the marked benefit which results from local applications over the cardiac region. When the heart is excited by emotion, the natural tendency is to place the hand over the heart, in order, as the phrase goes, "to still its beating." The pressure of the hand over the cardiac region certainly tends to quiet

palpitation, and the same result is obtained, even to a greater extent, by permanent pressure from the application of a plaster over this region. The plaster may be simply adhesive ; but I think the use of extract of belladonna is something more than a prejudice, and a belladonna plaster, I think, really has a more powerful action as a cardiac sedative than a merely adhesive plaster. A good deal depends upon the way the plaster is applied. It is best not to have it too small, and in the case of women it ought to be cut like

the pattern which I show you, so that it may fit over the breast. An india-rubber bag, filled with crushed ice, applied over the cardiac region sometimes quiets excessive cardiac action ; or, in place of it, a tube of india-rubber, coiled round and round, so as to form a flat plate through which cold water may be passed in a continuous stream, may have a similar action. When the action of the heart is feeble, a bag filled with hot water, or a warm poultice, a warm fomentation, or a turpentine stupe, may stimulate its action. In one case of cardiac disease I have seen ammonia liniment rubbed over the cardiac region for the relief of pain bring on such palpitation as to cause very great inconvenience to the patient, and to necessitate the relinquishing of the remedy.

Blisters.—In pericarditis blisters near or over the cardiac region are sometimes very useful both in checking the inflammation at its very commencement[21] and in causing absorption of fluid effused into the pericardium in acute pericarditis. Before the introduction of salicin,

the common method of treating inflamed joints in acute rheumatism was nearly to surround the limb, just above and below the joint, by a blister about an inch wide. This proceeding may possibly be regarded as a form of serum therapeutics, as it caused the urine previously acid to become alkaline.[22]

LITERATURE.

1 Lauder Brunton, "On the Use of Rest in Cardiac Affections," *Practitioner*, 1893, vol. li., p. 190.

2 Lauder Brunton, "On Posture and its Indications," *Lancet*, 2nd July 1892, p. 12.

3 J. Lionel Stretton, *Brit. Med. Journ.*, 1904, vol. ii., p. 927.

4 Lauder Brunton, *Practitioner*, vol. li., p. 202.

5 *Brit. Med. Journ.*, 23rd January 1892, p. 172.

6 *Lancet*, 5th April 1913, vol. i., p 970.

7 Lauder Brunton, *Atte dell' XI. Congresso Medico Internationale*, Roma, 29 Marzo–5th Aprile 1894; and *Brit. Med. Journ.*, 17th February 1912, p. 534.

8 Schott, *Berl. klin. Wochenschr.*, 1885; Th. Schott, *Berl. klin. Wochenschr.*, 1880; *Heilfactoren Bad Mannheims*, 1900, Wiesbaden; Bergmann, *Ueberanstrengung des Herzens*, 1898 (Wiesbaden: Bergmann); *Berl. klin. Wochenschr.*, 1896, No. 21; Literature, etc., Eulenburg's *Realencyclopedie*, 2nd ed., vol. xii.; *Verhand. d. XVI. Kongr. inn. Med.*, Wiesbaden, 1898; *Med. Rec.*, New York, 1901, 29th June, p. 1028.

9 Lauder Brunton, "Memoires en l'honneur du Prof. Raphael Lépine," *Rev. de Med.*, October 1911, p. 125 *et seq.*

10 M. J. Oertel, *Therapie des Kreisl. Storungen*, 1884 (Leipzig: Vogel); also v. Ziemssen's *Handbook*.

11 Oertel, *Ueber Terrain Curorte*, 1886 (Leipzig: Vogel).

12 Vaquez, *Bull. de la Soc. Med. des Hôp.*, 1905; Digne, *La cure de dechlorination chez les cardiaques*, Thèse (Paris, 1905); Bayer, *Arch. f. exp. Path. u. Pharm.*, 1907, vol. lvii., p. 162 *et seq.*; G. Etienne, *Archiv d. Maladies des Cœur*, 1908, vol. i., p. 129.

[13] Halliburton, in Schäfer's *Handbook of Physiol.*, 1898, vol. i., p. 130.
[14] Meilach, Thèse de Paris, 1889, quoted in Meyer and Gottlieb's *Experiment. Pharmacologie*, p. 299.
[15] Goulston, *Brit. Med. Journ.*, 1911, vol. i., p. 615.
[16] A. H. Carter, *Brit. Med. Journ.*, 1911, vol. ii., p. 1401.
[17] Winternitz. (Demonstration which I saw in his Klinik.)
[18] Lauder Brunton, 1882, *The Practitioner*, vol. xxix., p. 280.
[19] Lauder Brunton, "On Cardiac Diseases," 1897, *Edin. Med. Journ.*, vol. ii., p. 446.
[20] Lauder Brunton, *Clinical Society Reports*, vol. iii., 1870; and *Collected Papers*, First Series, p. 186.
[21] Lauder Brunton, *St Bartholomew's Hospital Reports*, 1875, vol. xi., p. 167 *et seq.*
[22] Herbert Davies, *Lancet*, 1865, vol. ii., pp. 127, 213, and 248.

CHAPTER XI

ACTION OF CARDIAC AND VASCULAR REMEDIES

Action of Drugs on the Circulation—Its Complexity—Means of Examining the Different Factors—Investigation of the Action of Drugs on the Frog's Heart — Different Reactions of the Inside and Outside of the Frog's Ventricle — Artificial Circulation through Mammalian Vessels; through the Mammalian Heart — Examination of the Effects of Poisons on the Heart and Vessels in the Body—General Rules regarding the Action of Drugs—Selective Action—Peripheral and Central Action—Effect of Dosage—Varying Composition of Drugs—Condition of the Body—Inurement—Temperature—Season—Climate—Necessity for Care in drawing Conclusions—Classification of Cardiac and Vascular Remedies—Cardiac Nutrients—Effect of Inorganic Salts on the Heart—Albuminous Substances — Sugars — Purin Bodies, Caffeine, etc. — Cardiac Tonics—Cause of Normal Tone.

Action of Drugs on the Circulation.—Diseases of the heart and circulation are capable of being benefited to an enormous extent by the proper use of drugs, but in order that these should do good only, and do no harm, a fairly exact knowledge of their mode of action is needful. But this is very difficult indeed to obtain, because

the action of drugs upon the circulation is exceedingly complex. What makes it all the more difficult is that pharmacology has outrun physiology so much that the action of drugs is now used to aid in the solution of some of the most difficult physiological questions. For example, it is impossible to ascertain by ordinary physiological methods whether the vagus contains accelerating as well as inhibitory fibres. When the vagus trunk is irritated, slowing or stoppage of the heart almost always occurs, and not acceleration. This result might be due to the absence of accelerating fibres, or to their action being masked by the superior power of accompanying inhibitory fibres.[1] By the use of atropine, however, the question of the presence of accelerating fibres along with the inhibitory has been completely settled, for this drug paralyses the peripheral terminations of the inhibitory fibres, and after its administration stimulation of the vagus trunk not only produces no slowing whatever, but actual acceleration. So complex is the action of drugs on the circulation, that it would have been impossible to ascertain the action of each on the heart and vessels separately, without the method, invented by Carl Ludwig, of artificial circulation.

Investigation of the Action of Drugs on the Frog's Heart.—In the winter of 1869, when H. P. Bowditch and I were both working in Ludwig's laboratory, I adapted the apparatus which he was using for the physiology of the frog's heart[2] to the examination of poisons upon it, by adding two small Marriott's vessels, one of

which, K, contained pure nutrient solution and the other, K′, poisoned solution (Fig. 86). The whole apparatus consisted of those two receivers, which fed a bent tube, BB′, having cannulæ

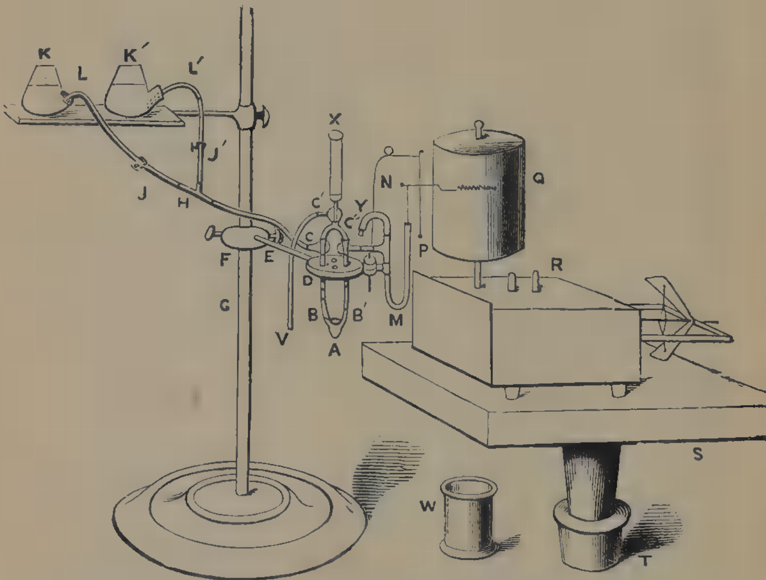


FIG. 86.—Apparatus for examining the action of drugs on the frog's heart. A is the heart with one cannula, B, tied into the vena cava, and another, B′, into the aorta. The nutrient fluid is driven from the aorta through the bent tube C into the vena cava, whence it passes on again through the heart. The beats are recorded by the manometer M on the recording cylinder Q. K and K′ are two Marriott's bottles, one containing nutrient fluid pure and the other poisoned. Either can be supplied to the heart at will through the tubes J and H connecting them with C.

attached to both ends. One of these, B, was inserted into the vena cava and the other, B′, into the aorta of a frog's heart, so that the fluid passed round the tube in an artificial circulation. To one side of this tube was attached a small

manometer, M, which recorded the movements of the heart on a revolving cylinder, Q. This apparatus I described and figured in the *British Medical Journal* in 1871.[3] In this apparatus the whole frog's heart was examined. A more elaborate one for examining the action of drugs on the frog's ventricle alone was described by Professor Kronecker in 1874,[4] and shown by him at The International Exhibition of Scientific Apparatus in London in 1876.[5] The apparatus was still further improved by Williams, who introduced valves allowing the fluid to circulate only in one direction.[6]

Different Reactions of the Outside and Inside of the Frog's Ventricle.—Mechanical stimulation of the outside of the frog's ventricle may be without effect, while stimulation of its inside may cause one contraction of the ventricle and three or four of the auricle. This shows a difference in sensibility between the two surfaces, and might be regarded as indicating the presence of reflex nervous centres in the heart which reacted differently to stimuli from these points.

There is also a difference in the action of the heart to poisons applied to the outside and inside of the ventricle. Thus strychnine applied to the outside of the frog's ventricle does not induce pulsation when its movements have been stopped by a ligature round the auriculo-ventricular groove. But if it is injected into the interior of the ventricle, it causes the pulsations to recommence; and if injected into the lymph sac so as to circulate in the blood before the ligature

is applied, it prevents the stoppage which would otherwise occur.*

It has been found by Schmiedeberg † and others that most cardiac poisons, digitalin and other members of the group, strophanthin, scillain, convallamarin, helleborein, bufotalin, and barium chloride, when applied to the outside of the ventricle cause standstill in diastole, which only passes into systole after sufficient time has elapsed for them to soak through the ventricle and reach its interior. But when injected into the interior of the heart or when they reach it through the general circulation, they at once cause increased systolic contraction and standstill in systole.

This curious result is explained by Schmiedeberg on the hypothesis that there are two kinds of muscular fibres in the frog's heart, one set contracting it (systolic fibres) and a second dilating it (diastolic fibres). The systolic fibres, he thinks, are innervated by the accelerator nerves, but are influenced by substances of the digitalis group in such a way that they contract more strongly and tend to remain contracted.

It seems to me that instead of ascribing this result to the presence of two antagonistic sets of muscular fibres, it might be more easily explained on the assumption that the muscular cells of the heart contract transversely as well as longitudinally (p. 86). If the power of muscular fibres or cells to contract transversely be assumed, it would serve, I think, to explain

* Brunton and Cash, *St Bartholomew's Hospital Reports*, 1880, vol. xvi., p. 230.

† Schmiedeberg, *Grund. d. Pharmakol.*, pp. 228-9.

not only active dilatation of capillaries, arteries, and veins, but of the heart. The refractory period in the heart might be also regarded as being one in which stimulation tended to cause transverse contraction of the cells.

Apparatus for Artificial Circulation in Mammalian Vessels.—In the summer of 1869

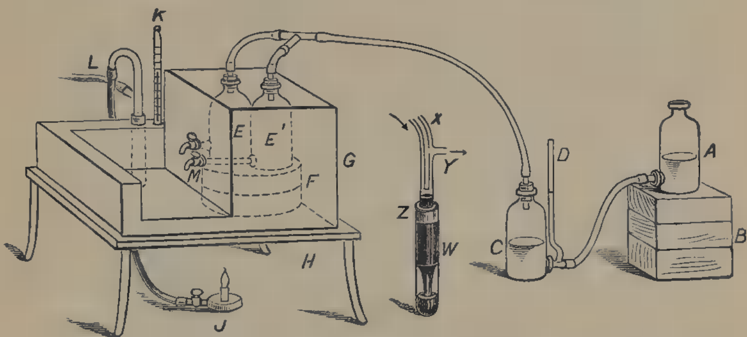


Fig. 87.—Apparatus for examining the effect of poisoned and unpoisoned blood in the rabbit's ear. This consists of two bottles, E and E′, one of which contains pure and the other poisoned blood. This is kept at blood-heat by the bottles being immersed in water in a tin vessel, G, heated by a gas-burner, J, with a regulator, L (shown also at W). The blood is passed from the tubes M into the carotid of a rabbit's severed head, which is also kept warm by the water-jacket. The pressure can be adjusted as desired by raising or lowering the bottle which contains mercury.

I examined, under the direction of Professor Ludwig, the contraction of arterioles throughout the body independently of the central nervous system.[7] In the winter of the same year he wished me to continue these researches, using artificial circulation of pure blood and poisoned blood to ascertain the effect of drugs upon the vessels. This apparatus I described, in 1871, in the *British Medical Journal*, and also Ludwig's

method of keeping up artificial circulation in frogs or mammals. These papers I afterwards republished in the form of a small book, which was, I believe, the first textbook of experimental pharmacology (*Experimental Investigations of the Action of Medicines*, 1875. London: Churchill).[8] Unfortunately I was prevented from carrying out the research, but it was continued by Mosso on other organs,[9] as Ludwig had reserved the rabbit's ear for investigation by me if ever I should be able to resume it.

Artificial Circulation through the Mammalian Heart.—As early as 1846 Ludwig had kept a mammalian heart alive,[10] apart from the body, by supplying it with blood from the carotid of another animal; but, so far as I know, this method was not further developed, either by himself or his pupils at Leipzig. It was again taken up by H. N. Martin[11] in 1881-1882, and has been utilised to a large extent by Langendorff.[12] By this method the descending aorta and subclavians are ligatured and all the veins excepting one jugular. Into one carotid a manometer is tied, and into the other a tube which connects that carotid with the jugular vein and represents the entire systemic circulation, as there is no other communication between the aorta and the right side of the heart. The blood then flows through the carotid and the jugular veins into the right heart, and is driven by the pulmonary artery into the lungs, which are kept in action by artificial respiration. By this apparatus the pressure in the aorta can be registered for hours together, and the heart

subjected to the action of any drug which it is wished to investigate. As a nutrient fluid defibrinated blood, alone or diluted with normal saline, may be used; but it is generally found more convenient to employ Ringer's fluid as modified by Locke and fully aerated by means of oxygen.[13]

General Rules regarding the Action of Drugs.—In trying to form a precise idea of the action of drugs upon the heart and vessels it is important to bear the following general rules in mind:—

(1) That—Drugs have a *selective* action on particular structures or tissues.

(2) That—Their action may be *peripheral*, or *central*, or both, and these two actions may either aid one another or counteract each other.

(3) That—Their action may be modified by the *dose*, and that large doses have sometimes exactly the opposite effect of small ones, small ones stimulating and large ones paralysing.

(4) That—The drug itself, which is supposed to be simple, may really be *compound*, and may contain components having actions antagonistic to each other.

(5) That—The action of the drug may be aided or interfered with by the chemical composition of the *blood* and tissues at the time of its administration.

(6) That—It may be interfered with by the cells or tissues of the body having become *inured* to the action of the drug.

(7) That—It may be interfered with by the *temperature* of the body.

It may be well now to take these rules one by one and consider them more fully.

(1) *Selective Action.*—The fact that drugs have a selective action on particular structures or tissues is well known to everyone who does microscopical work, for it is by means of the selective action of tissues for different stains that a great deal of our histological knowledge has been gained. It often happens that many tissues have an affinity for the same stain, but not to the same degree, so that if it is applied for a short time only, one tissue becomes stained, if for a longer time a second takes it up, and if for a longer time still, a third, and so on. Frequently the stain can be washed away from the tissues in inverse order. The same thing that can be seen with stains happens also with alkaloids and other drugs, where the effect is not visible to the eye, but can be discovered by other means.[14] Thus atropine has a peculiar affinity for the peripheral terminations of cerebro-spinal nerves going to involuntary muscles or glands, and in comparatively small doses it will paralyse them. The vagus belongs to this class of nerves, and its inhibitory fibres are paralysed by small doses. It paralyses other nerves of this class, and through its action on the third nerve it causes dilatation of the pupil; through the chorda tympani it causes dryness of the mouth, and these actions may even precede its effect upon the pulse. But when pushed still further it acts on the nerve centres, producing first excitement, and afterwards paralysis.[15] In mammals this action

usually causes death before the drug can act much upon the ends of motor nerves in voluntary muscle. This action may, however, be made out by the local application of the poisons to the muscle of a frog. Another poison, curare, has somewhat similar actions, but in an inverse order, for while comparatively small doses of it paralyse the ends of motor nerves in voluntary muscles, much larger doses are required to paralyse the vagus.[16] Nicotine appears to have a peculiar affinity for sympathetic ganglia, and to exercise on them a paralysing action; so that if a cerebro-spinal nerve ending in one of those ganglia is irritated between the ganglion and the spine (pre-ganglionic fibre), no effect is produced; but if the nerve passing from the ganglion to an organ (post-ganglionic fibre) is stimulated, it produces this effect as well after as before the poison.[17] The mode in which selective drugs act on nerves has been recently discussed by Dixon.[18]

An affinity of alcohol for the brain was recognised by Dr Percy in 1839,[19] as he found a much larger proportion in animals poisoned by it in the brain than in other organs. His observation regarding such an affinity has been confirmed and extended to other members of the aliphatic series.[20] Hans Meyer, in 1899,[21] propounded the theory that substances which, like most of this series, are soluble in fats, or fatty bodies (lipoids), must act on cells containing them, and especially on nerve cells, and thus exercise a narcotic action. This has been confirmed by Overton and others.

(2) *Peripheral and Central Action.* — The second rule is that the action of drugs may be peripheral, or central, or both. Indeed in most cases it is both, though in different degrees, as I have already mentioned. One can readily understand why it should be so, because both nerve centres and peripheral nerves contain substances of a more or less fatty nature (lipoid), and for such substances many alkaloids, as well as alcoholic and ethereal substances, have a special affinity.[22]

Central and peripheral actions may aid one another, as in the case of amyl nitrite, which has a dilating effect upon the vessels both by its action upon the nerve centres and upon the peripheral vessels themselves.[23]

On the other hand, the central and peripheral actions of a drug may oppose one another. Thus adrenalin stimulates the accelerating centres in the heart itself and thus tends to quicken the pulse. At the same time, by its peripheral action on the vessels it causes them to contract and produces a great rise of blood-pressure. This stimulates the inhibitory centre of the vagus and tends to slow the pulse. The rate of the pulse is therefore determined by the extent to which one or other of these factors prevails, and generally the pulse is first slow and then quick.

Caffeine stimulates the vaso-motor centre and thus tends to make the arterioles contract, but by its local action on the vessels themselves it tends to produce dilatation, and here again the blood-pressure will depend upon the balance between these two conditions.[24]

(3) *Effect of Dosage.*—The third rule is that the action may be modified by the dose, and large doses may sometimes have exactly the opposite effect of small ones. This is very well marked in the case of nicotine. Small doses stimulate the ends of the vagus in the heart and greatly slow the pulse, while larger ones completely paralyse these structures and make the pulse very quick. The same opposite effect of large and small doses is seen in the case of digitalis, although the *modus operandi* may be slightly different, for small doses slow the heart by stimulating the vagus roots, while large doses remove the inhibitory action of the vagus in the heart itself and thus render the pulse quick.[25]

Even atropine, which in very minute doses paralyses the ends of the vagus in the heart and renders the pulse quick, appears to have the opposite action when the dose is exceedingly minute, and slows the heart instead of quickening it. So minute is the dose required, however, that this action has been missed by many observers and its existence denied.[26] Opium as a rule tends to constipate; but when a large dose is injected directly into a vein in a dog, it produces most violent intestinal peristalsis, so that the fæces are evacuated so suddenly and in such quantity that, before laudanum was injected into the vein for the purpose of producing narcosis before an experiment in Ludwig's laboratory, a quantity of tow was placed at the anus of the animal in order to receive the excrement.

(4) *Varying Composition of Drugs.*—A drug

which is supposed to be simple may really be compound and may contain components having antagonistic actions. This, of course, is well known in regard to crude drugs such as opium, which contains many alkaloids, one of which, morphine, is purely soporific, while another, thebaine, has almost no soporific action, but is a pure convulsant like strychnine.[27] The same thing occurs in what is sometimes regarded as pure active principles. Thus muscarine, the active principle of the fly-fungus, has the remarkable power of stimulating the inhibitory apparatus in the heart and causing it to stand still in complete diastole.[28] This action is antagonised in the most complete manner by atropine.[29] But all specimens of muscarine are not equally pure, and most of them contain more or less of another substance, which has an action just like atropine and antagonises muscarine.[29] The action of any specimen of muscarine will therefore depend upon its more or less complete freedom from admixture with this other alkaloid.[30]

Digitalis itself probably contains at least four different principles which have an action somewhat alike but not identical, and the same is probably true of nearly all the substances belonging to the digitalis group.[31]

(5) *Condition of Body.*—The action of a drug may be aided or interfered with by the chemical composition of the blood and tissues at the time of its administration.

Thus Cash and I found that the poisonous effect of barium is not only counteracted to

some extent by potash administered at the same time, but by administration of potash for some days previously.[32] We found that beef tea counteracts the effect of barium on a frog's muscle;[33] but we made no experiments on its power to do so in the body. Hans Meyer found that the withdrawal of normal calcium

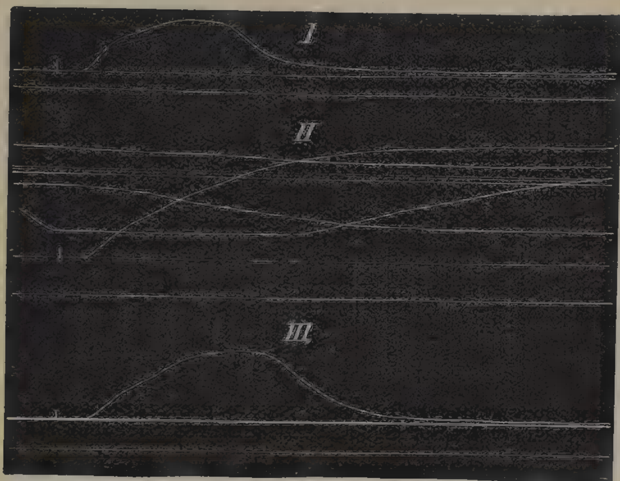


FIG. 88.

I. Curve of gastrocnemius in a frog in its normal condition.
II. Curve of the same muscle after immersion for 20′ in barium chloride solution 1-500.
III. Curve of the same muscle after immersion for 20′ in diluted Liebig's extract 1-300.

salts produces hyper-excitability of the sympathetic system towards adrenalin.[34]

(6) *Inurement.*—The action of a drug may be interfered with by the cells or tissues of the body having become inured to it. A well-known example of this is morphine, which in many persons when taken for a length of time

greatly loses its effect, so that the dose has to be constantly increased in order to obtain its usual effects. In this respect the effect of muscarine on the frog's heart is very extraordinary. If the heart be perfused with a solution containing muscarine it stops a long time in complete diastole. After some time it again begins to beat. If more muscarine is again added the same thing happens again, and this may be repeated several times. The apparent cessation of the action upon the heart is not due to the muscarine having been destroyed. For if the heart be taken after it has just begun to beat again for the first time, and the fluid it contains is washed out, enough muscarine may still be separated from the heart itself to produce its characteristic action upon another heart. It is thus clear that the action is not determined by the actual amount of poison present, but by its distribution.[35] This phenomenon becomes readily intelligible by the consideration of Ehrlich's schema of a cell. In the centre of a cell is protoplasm in a completely reduced state, at the periphery in a completely oxidised state, and between these two is a layer alternately more or less oxidised or reduced. The function of the cell depends upon the relative oxidation or reduction of its different layers.[36] If we suppose that the same occurs with poisons present in it we can readily see that as the poison becomes uniformly distributed through the cell its effect may cease, and that only the different proportion present in the outer layer or protoplasm will produce the effect.

(7) *Temperature.*—The action of drugs may be interfered with by the temperature of the body. Perhaps one of the most marked examples of this is digitalis, which at a high temperature completely loses its power of slowing the heart through the vagus.[37] Neglect of the temperature at which experiments have

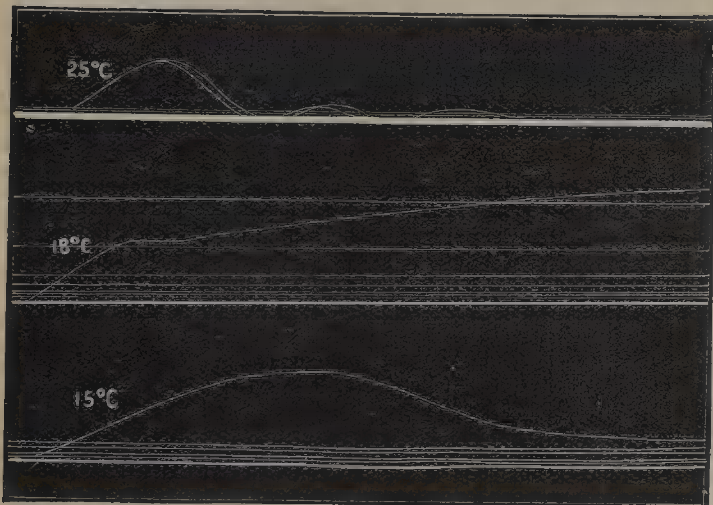


FIG. 89.—The lowest muscle curve is taken from a veratria muscle cooled to 15° C. The middle curve is taken from the same muscle at room temperature; the uppermost curves from the same muscle heated to 25° C. (Brunton and Cash.)

been made is one cause of the contradictory results which have frequently been obtained in the investigation of the action of different drugs. Thus atropine was found by Bowditch and Luciani to increase the systolic contraction of the frog's heart;[38] while Gnauck,[39] on the other hand, obtained an exactly opposite result,

and found that both atropine and hyoscyamine diminished ventricular contraction. At Kronecker's suggestion, the research was taken up anew by Schapiro,[40] who repeated the experiments at different temperatures, and found that both observers were right, and both were wrong. When the experiments were made at a low temperature, 7° to 8° C., atropine amplified the contractions of the heart, as stated by Bowditch and Luciani; but when the temperature rose about 15° C., atropine had an exactly opposite effect, and diminished the contractions, as stated by Gnauck.

Veratrine when applied to a frog's muscle at ordinary temperatures produces an extraordinary prolongation of the contraction, but this characteristic action is removed by heat or by cold.[41]

Effect of Season.—The effect of seasons of the year upon the antagonistic action of drugs in the body was observed by Luciani[42] and also by Ringer,[43] who found that while pilocarpine antagonises the action of muscarine, and atropine antagonises aconitine upon frogs in summer, it has no such action in winter.

Similar observations were made by Pantelejeff in regard to atropine and quinine.[44] In summer, quinine arrests the frog's heart in diastole; atropine subsequently administered causes the pulsations of the heart to recommence. In winter, quinine acts much more slowly upon the heart, and atropine increases instead of antagonising its action.

Climate.—The opinion expressed by various authors, that the action of drugs may be largely varied by climate, has often been received with distrust. There seemed to be no very definite reason for supposing that climate should exercise this action, and so any difference that might exist was apt to be ascribed to other causes. The statement of Lisfranc, that the inhabitants of southern climates tolerate much larger doses of barium than those of northern climates, is at first sight curious, and one may be inclined to be sceptical regarding it. There seems no obvious reason why an inorganic substance like barium should act differently in Italy and in England, although one might be inclined to grant that such a modification might perhaps occur in the case of more complex and less stable organic substances. The marked effect of heat upon voluntary muscle poisoned by veratrine, however, seems to indicate that the resistance opposed to the action of the drug by inhabitants of warmer countries may be due to the higher temperature, and Cash and I have found experimentally that cold retards the fatal effect of barium upon guinea-pigs.[45]

Necessity for Care in drawing General Conclusions.—Contradictory statements regarding the action of drugs have sometimes been due to different observers employing animals of different kinds or of different species in their experiments, and concluding that the results they obtained were applicable to all

animals. Thus Johannsen[46] found that caffeine caused rigidity in the muscles of frogs. Aubert[47] found that it did not. This difference of result, according to Schmiedeberg,[48] was due to the employment of Rana temporaria by Johannsen and of Rana esculenta by Aubert. Morphine acts as a narcotic in most animals, but on pigeons it acts as an antipyretic.[49]

Classification of Cardiac and Vascular Remedies.—These may be divided into six classes :—

1. Cardiac nutrients.
2. Cardiac tonics.
3. Cardiac stimulants.
4. Cardiac depressants.
5. Vascular contractors.
6. Vascular dilators.

In addition to these we have a number of drugs which have a less direct action upon the heart and vessels themselves, but rather affect tissue change and the composition of the blood, and influence the heart indirectly through other organs. Thus digestives, and eliminants both by the bowels and kidneys, are important adjuncts to the drugs which act directly upon the circulation.

Cardiac Nutrients.—The best nutrient for the heart is, of course, well aerated blood, with a proper proportion of nutrient matter and few waste products. The action of nutrient materials has been investigated by experiments both upon the frog's heart and upon the mammalian heart by methods which we owe to Carl Ludwig. In the first experiments made by him and his pupils on the frog's heart, serum was

used, and later a simple solution of common salt (NaCl) about ·5 to ·6 per cent.,[50] that is to say about two and a half grains to the ounce, was circulated artificially through the frog's heart. For a length of time it continued to beat, but gradually the pulse became slower and feebler and at last ceased. The addition of diluted blood increased the strength and made it beat for a longer time,[51] and when it stopped, the stoppage was not due to exhaustion of the nutrient material but to accumulation of waste products, so that when these were washed out with saline solution containing a very small quantity of sodium carbonate, the heart began to beat again.[52]

Effect of Inorganic Salts upon the Heart.—An interesting and important discovery was made by Ringer, who found that when the saline solution was made with tap-water it maintained the action of the heart for a very much longer time than when made with distilled water.[53] On investigating the cause of this, he found it was the lime in the tap-water which had a stimulating effect upon the heart, and he was able to produce nearly the same effect by adding lime in small quantities to saline solution made with distilled water.[54] But if the heart be perfused with saline and calcium alone the diastole tends to become less and less, and finally the heart stands still in a condition of systole.[55] If a small quantity of potassium be added to this solution the diastole becomes more complete and the heart goes on acting in a very perfect manner. If the proportion of

potassium, however, be too large, the diastole becomes greater and greater, and finally the heart stands still in complete diastole.[56] To maintain rhythmical contraction, a proper proportion is required between the salts of Na, K and Ca in the nutrient fluid.[57] There seems to be a close relationship between the presence of potassium in the nutrient fluid and the action of the vagus. Excess of potassium and stimulation of the vagus both cause the heart to stop in diastole. If the potassium be thoroughly washed out of the heart by means of normal saline, the vagus loses its inhibitory power, and if the amount of potassium in the perfused fluid entering and leaving the heart be estimated during vagus irritation it is found that the quantity leaving the heart is increased, the stimulation of the nerve having apparently caused such dissociation as to free the potassium and to allow of its removal. It is not improbable that the whole question of the mode of action of the vagus, and of the transmission of stimuli through the A-V bundle may finally turn out to be a chemical one.[58]

Albuminous Substances.—It has been shown by Kronecker[59] that although a heart supplied with salts alone may continue beating for a length of time, yet it becomes much more quickly exhausted than if albuminous substances of the proper character are supplied to it.

It is not every kind of albuminous substance which will act as a nutrient. Serum albumen does so, but neither egg albumen, casein of milk, syntonin, nor peptone act as nutrients.[60]

Sugars.—Amongst the most powerful cardiac nutrients appears to be glucose; for Locke found in his experiments that the addition of glucose, even in very small quantity, to a saline fluid greatly increased its nutritive effect on the isolated mammalian heart.[61] Other sugars have less action. Their nutritive effect apparently runs parallel with their susceptibility to fermentation, glucose standing far ahead of the others.[62]

Sugar Treatment of Failing Heart.—The nutritive power of sugar has been utilised in cases of cardiac weakness by Dr Goulston, and the effects of large quantities of sugar administered daily are sometimes extraordinarily good. The mode of administration was suggested by Dr Goulston [63] and is described more in detail by Dr Carter.[64] It consists in making the patient abstain from acids, fats, fruits and sauces, and giving two ounces of sugar daily the first week, three ounces the next, and four ounces the next again. This quantity may be kept up or increased. The form of sugar used was "Glebe granulated" cane sugar. Probably other forms of pure cane sugar would answer quite well. I have, however, tried honey in place of sugar, but was obliged to discontinue it because it caused acidity in the stomach.

Purin Bodies.—We know that a fire when allowed to burn without attention will often go out before the whole of the coal is consumed, because it is smothered in its own ash, and that if we heap ashes on the fire we tend to put it out. But the result is different if we use cinders

instead of ash; and although cinders represent half-burned coal, they are sometimes very useful in keeping up a fire or in helping it to burn when it is low. In the same way the ashes, as we may term them, of the tissues tend to smother the vital fires, and to prevent the tissues from performing their proper functions; but the vital cinders, that is, substances which are derived from albumens and are on the way to urea or uric acid, may be very useful.

Amongst these we have a series of bodies to which the term of purin bodies has been applied — xanthine, hypoxanthine, methylxanthine, dimethylxanthine or theobromine, and trimethylxanthine or caffeine. All these bodies are probably injurious in large quantities, but just as a few cinders may help a fire, so when used in small quantities they are often very useful. Beef-tea and extracts of meat have little or no nutritive action, and life cannot be sustained upon them, but they are useful stimulants, as was shown by Parkes in the Ashanti campaign;[65] and in disease they act as cardiac stimulants, though only slightly as cardiac nutrients. Caffeine in large doses acts as a muscular poison, and tends to cause strong contraction, ending in rigor of the muscle.[66] Its effect in small doses upon the heart appears to be that it increases the muscular contraction and strengthens the ventricular beats.[67]

Cardiac Tonics. Cause of Normal Tone.— Like other involuntary muscles, such as the bladder, the heart possesses the quality of tone,[68] which may be said to be the outer limit of its

ordinary dilatation. In the bladder we find that urine may gradually accumulate up to a certain point without either causing discomfort or desire to micturate, but if filled beyond that point one or other of these sensations comes on. Yet if micturition is prevented the desire to empty the bladder may pass off, and it may go on filling still more till it is distended to a considerably greater size before the desire to micturate again comes on. The bladder would thus seem to have a tone which can be fixed at various points, and something of the same occurs in the case of the heart. The healthy heart only dilates up to a certain point and then contracts, but the same heart may undergo considerable dilatation and then with an increased capacity may go on beating as before. The tone of the normal heart appears to be maintained by the internal secretions of certain glands, and especially of the suprarenal glands,[69] and possibly of the pituitary bodies which are more or less constantly poured into the blood. Adrenalin is constantly present in normal blood serum,[70] and its power to cause arterial contraction is shown by the fact that when strips of artery are put into Ringer's solution they contract on the addition of normal serum to it.[71] The amount of adrenalin in mixed blood is smaller than in the blood of the suprarenal vein. In diseases of the suprarenal gland, when the medullary portion alone is affected, the heart loses both its tone and contractility and the arterial pressure is greatly reduced, but there is no discoloration of the skin, whereas if the cortical substance is

affected the peculiar bronzing characteristic of Addison's disease occurs in addition.[72]

LITERATURE.

[1] Schmiedeberg, *Ber. d. sächs. Gesellsch. d. Wiss., math.-phys. Cl.*, 1870, p. 135 *et seq.;* and *Ludwig's Arbeiten*, 1870, p. 46.

[2] Bowditch, *Ber. d. sächs. Gesellsch. d. Wiss., math.-phys. Cl.*, 1871, p. 655; and *Ludwig's Arbeiten* for 1871, p. 142.

[3] Lauder Brunton, *Brit. Med. Journ.*, 1871, vol. ii., p. 687; *Collected Papers on Circulation and Respiration*, p. 305; and *Experimental Investigation of the Action of Medicines*, p. 72 (London: Churchill, 1875).

[4] Kronecker, *Beiträge z. Anat. u. Physiol. Festgabe*, Carl Ludwig gewidmet, Leipzig, 1874, pp. 174 and 175.

[5] Kronecker, *Catalogue of Scientific Appliances*, Exhibition at South Kensington, 1876.

[6] F. Williams, *Arch. f. exp. Path. u. Pharm.*, 1880, vol. xiii., p. 1.

[7] Lauder Brunton, *Bericht. d. math.-phys. Classe der königl. sächs. Gesellsch. d. Wiss.*, 1869, p. 285; and *Ludwig's Arbeiten*, 4ter Jahrg. für 1869, p. 101.

[8] Lauder Brunton, *Brit. Med. Journ.*, 1871, 3rd June, vol. i., p. 581, etc.; *Experimental Investigation of the Action of Medicines*, p. 84 *et seq.* (London: Churchill, 1875).

[9] Mosso, *Ludwig's Arbeiten*, 1874, p. 305.

[10] Carl Ludwig, *Ztschr. f. rat. Med.*, 1846, vol. v.

[11] H. Newell Martin, *Phil. Trans.*, 1883, vol. clxxiv., p. 666.

[12] Langendorff, *Pflüger's Archiv*, 1895, vol. lxi., p. 291.

[13] Locke, *Journ. of Physiol.*, 1895, vol. xviii., p. 332; Ringer, *ibid.*, vol. iii., 1880-82, p. 380, vol. iv., 1883-84, pp. 29 and 222.

[14] Ehrlich, *Therap. Monatsh.*, März 1887, p. 90.

[15] Nothnagel and Rossbach, *Arzneimittellehre*, p. 755, 6th Aufl. 1887; V. Bezold, *Untersuch. d. Physiol. Labor.*, Würzburg, Bd. i.; Schmiedeberg, *Ludwig's Arbeiten*, 1870; Schmiedeberg, *Grundriss d. Pharmakol.*
[16] Cl. Bernard and Pelouze, *Compt. rend.*, 1850, vol. xxxi., p. 533; Bernard, *Leçons s. l. Effets des Substances Toxiques*, p. 329 (Paris, 1857); Tillie, *Arch. f. exp. Path. u. Pharm.*, 1890, vol. xxvii., p. 27.
[17] Langley and Dickinson, *Journ. of Physiol.*, 1890, vol. xi., p. 278; Langley (pre-ganglionic and post-ganglionic fibres), *ibid.*, 1894, vol. xv., p. 178; and Langley, Schäfer's *Textbook of Physiol.*, 1900, vol. ii., p. 616 *et seq.*
[18] Dixon and Ransom, *Ergeb. d. Physiol.*, 1912, 12th Jahrb., p. 765 *et seq.* (Wiesbaden: Bergmann).
[19] Percy, *An Experimental Enquiry concerning the Presence of Alcohol in the Ventricles of the Brain after poisoning with that liquid, together with Experiments illustrative of the Physiological Action of Alcohol* (London, 1839).
[20] Authors quoted by Hans Meyer, *Arch. f. Exp. Path. u. Pharm.*, 1899, vol. xlii., p. 109 *et seq.*
[21] Hans Meyer, *op. cit.* and *ibid.*, 1901, vol. xlvi., p. 338.
[22] E. Overton, *Studien über Narkose* (Jena: Fischer, 1901). Literature, Meyer and Gottlieb's *Pharmakologie*, p. 90, etc.
[23] Lauder Brunton, *Ludwig's Arbeiten*, 4th Jahrg. for 1869 (Leipzig, 1870), p. 111; Filehne, *Arch. f. Anat. u. Physiol.*, 1879, p. 386; and *Pflüger's Archiv*, 1874, vol. ix., p. 470.
[24] Gottlieb, *op. cit.*, pp. 213 and 233.
[25] Traube, *Charité Annalen*, 1851, and *Gesammelte Beiträge*, 1871, vol. i., p. 194 (Hirschwald: Berlin).
[26] Nothnagel and Rossbach, *Arzneimittellehre*, p. 763, 6th Aufl. (Berlin, 1887).
[27] Claude Bernard, *Compt. rend.*, 1864, vol. lix., p. 413. Crum-Brown and Fraser, *Trans. Roy. Soc.*, Edinburgh, 6th Jan. 1868. For literature, see H. C. Wood, *Therapeutics*, 8th ed., p. 177 (Philadelphia, 1891); and Th. Husemann, *Arch. f. exp. Path. u. Pharm.*, 1878, vol. ix., p. 414 *et seq.*

[28] Schmiedeberg u. Koppe, *Das giftige Alkaloid des Fliegenpilzes* (Leipzig, 1869).
[29] Schmiedeberg, *Ludwig's Arbeiten* for 1870, p. 45.
[30] Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, 1881, vol. xiv., p. 377.
[31] Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, 1875, vol. iii., p. 18.
[32] Brunton and Cash, *Ueber vorbeugende Gegengifte*, *Centralb d. med. Wiss.*, 1884, p. 545.
[33] Brunton and Cash, *St Bartholomew's Hospital Reports*, 1885, vol. xx.
[34] Hans Meyer, *Brit. Med. Journ.*, 1910, vol. ii., p. 1594.
[35] Straub, *Pflüger's Archiv*, 1907, vol. cxix., p. 127.
[36] P. Ehrlich, *Das Sauerstoff Bedürfniss des Organismus* (Berlin : Hirschwald, 1885).
[37] Brunton and Cash, *Practitioner*, 1884, vol. xxxiii., p. 272.
[38] Luciani, *Ludwig's Arbeiten* for 1872, p. 187.
[39] Gnauck, *Ver. d. physiol. Gesellsch. zu Berlin*, 1881.
[40] Schapiro, *Centralb. d. med. Wiss.*, 1884, p. 577.
[41] Brunton and Cash, *Journ. of Physiol.*, 1883, vol. iv., p. 1.
[42] Luciani, *op. cit.*, p. 187.
[43] Ringer, *Journ. of Physiol.*, 1880-82, vol. iii., p. 115.
[44] Pantelejeff, *Centralb. f. d. med. Wiss.*, p. 529, 1880.
[45] Brunton and Cash, *St Bartholomew's Hospital Reports*, 1885, vol. xx.
[46] Johannsen, *Diss. Dorpat*, 1869, quoted by Schmiedeberg.
[47] Aubert, *Pflüger's Archiv*, 1872, vol. v., p. 598.
[48] Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, 1874, vol. ii., p. 62 *et seq.*
[49] Brunton and Cash, *Centralb. d. med. Wiss.*, 1886, p. 241 ; and *Beiträge zur Physiol.*, Carl Ludwig zu seinem siebzigsten Geburtstage gewidmet von seinen Schülern, 1887, p. 149 *et seq.* (Leipzig : Vogel).
[50] *Ludwig's Arbeiten* for 1866, p. 80 ; for 1869, p. 178 ; for 1870, p. 44 ; for 1871, p. 144 ; for 1872, p. 114.
[51] Rossbach, *Ludwig's Arbeiten* for 1874, p. 94 ; Stiénon, *ibid.*, 1878 ; and *Arch. f. Anat. u. Physiol.*, 1878, p. 269.
[52] Merunovicz, *Ludwig's Arbeiten* for 1875, p. 173 *et seq.*

[53] Ringer, *Journ of Physiol.*, 1885, vol. vi., p. 362.
[54] Ringer, *op. cit.*, p. 381.
[55] C. W. Greene, *Amer. Journ. of Physiol.*, 1899, vol. ii., p. 102.
[56] Ringer, *op. cit.*, 1880-82, vol. iii., p. 389.
[57] Howell, *Amer. Journ. of Physiol.*, 1899, vol. ii., p. 80.
[58] Howell and Duke, *Amer. Journ. of Physiol.*, 1908, vol. xxi., p. 51.
[59] Kronecker, *Ludwig's Festgabe*, 1874, p. 200.
[60] Martius, *Archiv f. Anat. u. Physiol.*, *physiol. Abt.*, 1883, p. 562; and *Kronecker's Arbeiten*, 1883.
[61] Locke, *Journ. of Physiol.*, 1895, vol. xviii., p. 332.
[62] Locke, *Centralb. f. Physiol.*, 1901, vol. xiv., p. 670; Proc. of Physiol. Soc. in *Journ. of Physiol.*, vol. xxxi., p. xiii.; Locke and Rosenheim, *Journ. of Physiol.*, 1907, vol. xxxvi., p. 205.
[63] Goulston, *Brit. Med. Journ.*, 1911, vol. i., p. 615.
[64] Carter, *Brit. Med. Journ.*, 1911, vol. ii., p. 1401.
[65] E. A. Parkes, *On the Issue of a Spirit Ration during the Ashanti Campaign* (London: Churchill, 1875).
[66] Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, 1874, vol ii., p. 62; Brunton and Cash, *Journ. of Physiol.*, 1888, vol. ix., p. 112.
[67] Dreser, *Arch. f. exp. Path. u. Pharm.*, 1888, vol. xxiv., p. 240.
[68] Gaskell in Schäfer's *Textbook of Physiol.*, 1900, vol. ii., p. 194.
[69] Cybulski, abstract in *Centralbl. f. Physiol.*, 1895, vol. ix., p. 174.
[70] Ehrmann, *Arch. f. exp. Path. u. Pharm.*, 1905, vol. liii., p. 110.
[71] Douglas Cow, *Journ. of Physiol.*, 1911, vol. xlii., p. 132.
[72] Gibson, *Brit. Med. Journ.*, 27th July 1912, p. 167. For a full account of the suprarenal bodies, with literature, *vide* Swale Vincent, *Internal Secretion and the Ductless Glands* (London: Edward Arnold, 1912), and *The Internal Secretory Organs: Their Physiology and Pathology*, by Prof. Artur Biedl, Transl. by L Forster, 1912. (London: John Bale, Sons, and Danielsson).

CHAPTER XII

ACTION OF CARDIAC TONICS

Cardiac Stimulants — Digitalis — Historical Sketch — Action of Digitalis on the Frog's Heart—Action of Cardiac Tonics on the Embryonic Heart—Action of Digitalis on Mammals—On the Mammalian Heart—On the Arterioles—Stages in the Action of Digitalis—Toxic Action of Digitalis—Action of Digitalis on the Kidney—Résumé of the Action of Digitalis—Uses of Digitalis—Action of Digitalis on Œdema—Congeners of Digitalis—Differences between Digitalis and other Cardiac Tonics—Drawbacks to the Action of Digitalis and other Cardiac Tonics—Removal of these Drawbacks—Digitalis in Cases of Fatty Heart—Action of Adrenalin on the Heart and Vessels—Action of Camphor—Action of Strychnine on the Heart—Action of Caffeine and other Purin Bodies—Action of Pituitary Gland.

Cardiac Stimulants.—It is almost impossible to draw a sharp line between cardiac tonics and cardiac stimulants, as the same drugs that tend to maintain cardiac tone and prevent excessive dilatation have also the power of increasing the contractile power of the heart in its ordinary pulsations. The most typical example of this class of drugs is digitalis. There are, however, many other plants which possess active principles very nearly allied to those of digitalis and

having a physiological action more or less like it. It is now generally recognised that digitalis has (1) the power of slowing the heart, (2) of making it stronger, (3) and of contracting the vessels.

Historical Sketch of the Action of Digitalis. —It is only, however, within the last half-century that this view has been adopted. So long ago as 1839, James Blake, at Professor Sharpey's suggestion, made some manometric experiments with digitalis. By injecting infusion of digitalis into the carotid, so that it passed into the general circulation before reaching the heart, he found it produced a very great rise in the arterial tension, and therefore concluded that it contracted the capillaries.[1] His experiments attracted little attention, and no additions were made to our knowledge of the drug until Traube began the remarkable series of experiments which laid the foundation for an accurate knowledge of its mode of action, and consequently of its therapeutical application. Traube found that it slowed the heart and increased the blood-pressure. He proved that this slowing was due to a central action upon the vagus, but he attributed the rise of blood-pressure entirely to increased action of the heart.[2] That such action does contribute to the rise of blood-pressure there can be little doubt, but it is not the main cause. Traube also discovered, in 1865, that digitalis had an action on the vaso-motor nerves (Digitalis wie ich nachträglich gefunden habe, auch auf das vasomotor Nervensystem erregend wirkt).[3] To him, therefore, belongs the priority of the discovery of the

action of digitalis on the arterioles as well as on the heart; and, taken along with his previous work, this passage shows that he had obtained a complete knowledge of the action of the drug, yet he did not formulate it in its entirety until 1871.[4] I think, therefore, that the first complete description of the physiological action of digitalis is that which I gave myself in the thesis which I presented to the University of Edinburgh in 1866.[5] I subjoin here the chief points of this thesis, which I communicated to my friend Professor Rutherford, and which he published in *The Journal of Anatomy and Physiology*, vol. i., 1867, p. 154. "It acts as a diuretic even in health. Poisonous doses first occasion diminished frequency, but increased strength of the cardiac pulsations, together with contraction of the capillaries. The slackening of the heart's speed is due to the direct action of poison upon the heart, and not to the increased resistance offered by the contracted capillaries. After a short time the pulse becomes irregular, the capillaries dilate, the arterial tension diminishes, and syncope is apt to supervene. Lastly, the pulse becomes very rapid, and stoppage of the heart in a state of contraction soon follows."

Action of Digitalis on the Frog's Heart.—Its action upon the heart of the frog is very marked and characteristic, and the action here is less complicated than in mammals, inasmuch as the heart itself is less under the control of the central nervous system, and is less readily affected by alterations which may occur in the vessels. When the excised heart of a frog is

either laid in a solution containing the active principles of digitalis, or is connected with an apparatus by which serum containing these principles may be circulated through it, changes are observed, which may be divided into changes in rate of pulsation and changes in character of pulsation. The heart first of all begins to pulsate more slowly, and at the same time more powerfully; the contractions become gradually stronger, and the relaxation or diastole becomes less perfect, so that finally the heart stands still altogether in a state of complete contraction. If the heart which is thus standing still be forcibly dilated, by passing fluid into its interior under pressure, pulsation will recommence.[6] Occasionally during the process of contraction small points on the surface of the heart may be observed, which remain dilated, and look like small purple pulsatile pouches on the surface of the organ.[7] The nature of these pouches has not been definitely ascertained, but it is not improbable that they are due to slight injury of the muscular fibre in the process of removing the heart from the body of the frog. When the heart of a frog is left *in situ*, and is merely exposed to view by opening the thorax of the animal and dropping a solution of digitalis upon it, the same phenomena are observed. They are unaltered by the use of atropine, and are supposed to be due to the action of the drug upon the muscular fibres of the heart itself.

Mode of Action of Cardiac Tonics on the Embryonic Heart; Relation of their Action

to Oxidation.—J. W. Pickering has found that digitalis has the same action on the embryonic as on the adult heart, rendering the systole very powerful and the diastole imperfect, so that at last the heart stops in tonic contraction, and becomes very pale. Caffeine slightly increases both the frequency and energy of the systoles, and finally causes stoppage in systole.[8] He points out (p. 436) that the action of these two drugs on the heart may be due to their effect upon oxidation,[9] for they are *par excellence* the drugs which produce tonic contraction, and as Cash and I have shown, they accelerate the oxidation of protoplasm.[10] Other drugs which retard oxidation tend to produce an atonic condition of the embryonic heart.

Action of Digitalis in Mammals. — In mammals, digitalis causes increased contraction of the muscular fibres, both (1) in the heart, and (2) the arteries. This increased contraction appears to be partly due to the action of digitalis on the muscular fibres themselves, but its effect upon the muscle is greatly modified by its action upon the nervous system. Its action is exerted especially upon the medulla oblongata, and it appears to affect first the inhibitory centre of the vagus and the vaso-motor centre for the vessels. When small doses are given, the effect appears to be limited to these centres, but when the administration is carried to the extent of poisoning, the adjacent respiratory and vomiting centres are also affected.

Action of Digitalis on the Mammalian

Heart.—The action of digitalis on the mammalian heart when isolated from the body and perfused with a nutrient solution is to first slow and then accelerate its pulsations.[11] It increases the force as well as the frequency of its systolic contraction,[12] and at the same time it causes the dilatation during diastole to become more complete, so that the actual work done by the heart may be increased to more than three times its former amount.[13]

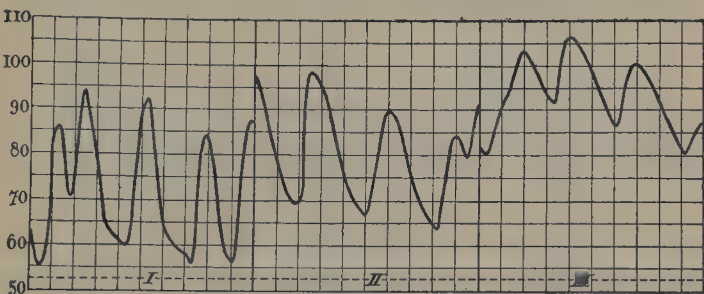


FIG. 90.—Kymographic tracings of the blood-pressure in a dog under the influence of digitalis. *I.* shows the normal curve, *II.* and *III.* show the slowing of the pulse and rise of blood-pressure produced by the drug. (Brunton and A. B. Meyer.)

Action of Digitalis on Arterioles.—The rise of blood-pressure which digitalis produces was attributed by Traube and von Bezold to increased action of the heart, and they left the arterioles altogether out of account as a factor in its production. In my thesis, presented to the Edinburgh University in 1866, I pointed out the importance of the arterioles, and in the winter of 1867-68 I obtained, in conjunction with A. B. Meyer, experimental evidence of

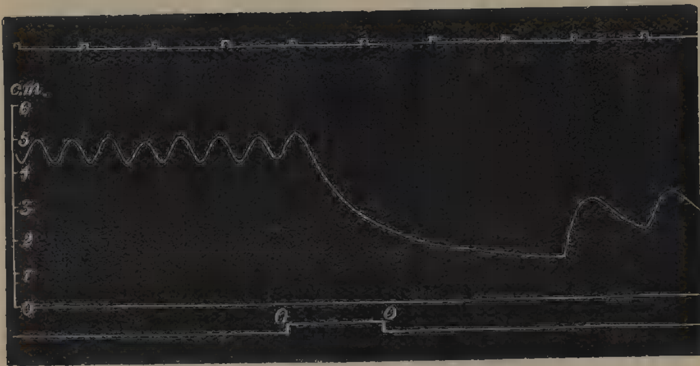


FIG. 91.—Normal tracing of the blood-pressure in a dog during stoppage of the heart by electrical stimulation of the vagus. *O O* marks the duration of the stimulation. It will be noticed that during the stoppage the blood-pressure falls to within 1·5 cm. of the abscissa. The latent period of the vagus is also shown, a complete pulse occurring between the commencement of stimulation and stoppage of the heart. The long duration of the vagus action is also shown, pulsation not recommencing until a considerable time after stimulation has ceased.

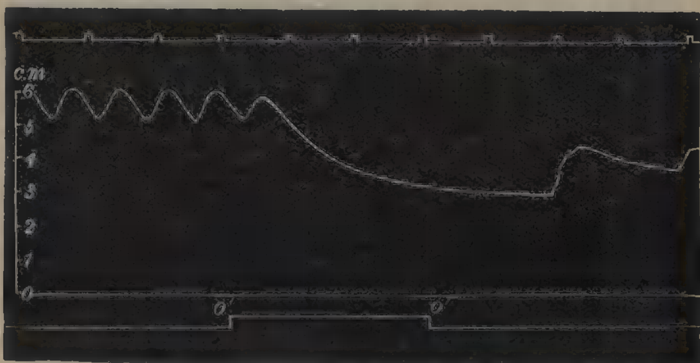


FIG. 92.—The same experiment as in Fig. 91, but after the injection of digitalis. Although the arrest of the heart is longer than in the previous experiment, the blood-pressure only falls to within 3 cm. of the abscissa instead of to 1·5 cm. The action of digitalis is also seen in the slower and larger beats before the heart stops.

this action, using the identical kymograph which Traube had employed.[12] We noticed that after the injection of digitalis into the veins of a dog, the pressure in the arteries not only rose higher than before, but it fell more slowly during diastole. Had the arterioles not been contracted, the higher pressure would have driven the blood more quickly through them in diastole, and so the fall would have been quicker than before, instead of being slower, as we found it to be. In order to obtain more certain proof of this, however, I then took up the question along with Dr Tunnicliffe, and instead of using the normal systole of the heart we prolonged it greatly by irritation of the vagus. The results we arrived at entirely confirmed my previous observations; for, although the pressure was considerably raised in the arteries by the administration of digitalis, it fell very much more slowly than in the normal animal, while the heart was standing still from irritation of the vagus. I need not enter further into the discussion of this point, as Tunnicliffe and I have gone fully into it in our paper.[13]

Stages in the Action of Digitalis. — The action of the drug may be divided into several stages. These stages have been variously described, so that the stages of different authors do not correspond. The essential part of the division is that in the first stage there is increased power, both of those parts of the nervous system connected with the heart and vessels and of the muscular fibres in them, while in the later stages

more or less complete paralysis of these structures occurs.

We might, then, take as the—

1st stage, that in which there is *increased action* in all the nervous and muscular structures concerned in the circulation;

2nd, that in which the *nervous system* of the

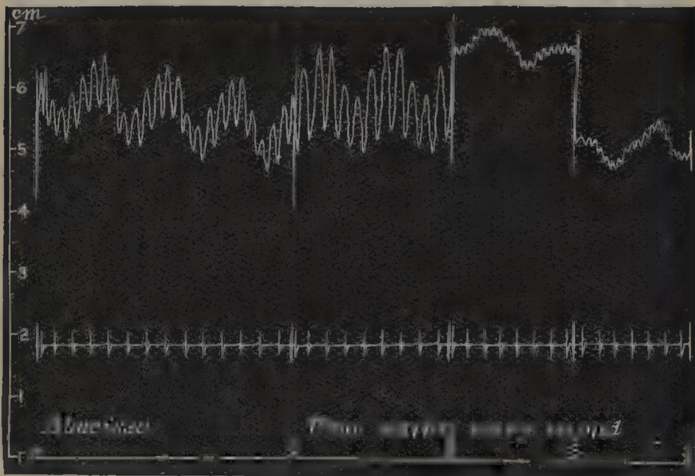


FIG. 93.—Tracing of blood-pressure showing the effect of digitalis. Section 1, normal; 2, slowing of heart, slight rise of blood-pressure; 3, paralysis of vagus, rapid pulse, greater rise of pressure; 4, dilated vessels and fall of blood-pressure. (Brunton and Tunnicliffe.)

heart begins *to fail*, while muscular power and the whole vascular apparatus are still intact;

3rd, that in which the *muscular fibre* of the heart begins *to fail*;

4th, that in which the *vessels* become *enfeebled*.

In the first stage (Section 2, Fig. 93) we have a rise of blood-pressure and usually a slowing of the

pulse, this slowing being due to the action of the drug both on the vagus roots and ends in the heart. Although the pulse is slow, the systole of the heart is not prolonged, and there is, therefore, a much longer diastole during which the heart is able to rest. The blood-pressure in the kidneys is increased as well as in the other organs, and the urinary secretion is therefore augmented. In the second stage (Section 3, Fig. 93) while the blood-pressure continues high, the vagus becomes partially paralysed, and therefore the pulsations become at first irregular and afterwards very rapid. In this condition spasm of the renal vessels may occur, and the urinary secretion may entirely cease. When this occurs in man, the condition of the patient is dangerous. In the third stage (Section 4, Fig. 93) the heart becomes feebler, and may again become regular, from failure either of the muscular fibre itself or the intrinsic ganglia. The arterioles now relax, the blood-pressure begins to fall, and the urine may again become copious. In the fourth stage, the vessels dilate generally, blood-pressure falls very greatly, and the heart stops sometimes in systole, as in the frog, but very frequently in díastole.

Toxic Action of Digitalis.—When pushed too far it produces poisoning, and one of the first symptoms is nausea and vomiting. This may be due simply to extension of the irritation in the medulla from the vagus and vaso-motor centres to the vomiting centre; but it may be due also, to some extent, to a local irritation of the stomach by the digitalis being secreted into

it, in the same way as tartar emetic, or the toxins of cholera. In medical practice, gastric irritation is usually one of the first indications that the physiological effect of digitalis is passing into its toxic action. Sometimes, however, the pulse becomes abnormally slow, even before sickness occurs. If the warning given either by sickness or by the pulse is attended to, and the administration of the drug is stopped, usually no further disadvantage occurs; but if these warnings be unheeded, the vagus becomes paralysed, the pulse becomes irregular or abnormally rapid (Fig. 93), excessive vomiting may set in, collapse may occur, and the secretion of urine may be entirely arrested. The secretion of urine may cease at the time when the blood-pressure is at its maximum, as I found along with Mr Power in the case of digitalis,[14] and along with Mr Pye in the case of erythrophlœum[15] (Fig. 99). The stoppage of secretion is exactly like that which occurs from ligature of the renal artery, and in all probability it is due to spasm of these arteries stopping the circulation through the kidney.[14] As the pressure begins to fall and the arteries relax, urine is again secreted, but it is often albuminous, exactly like the urine secreted after the arteries have been ligatured and then released.[14]

In the case of poisoning by digitalis which I described in my thesis, the pulse had been extremely rapid before I saw the patient. When I took the first tracing (Fig. 94) the vagus, which had been paralysed, was beginning to reassert its power over the heart, and although

the pulse was still quick, occasional slow beats were interposed. As the vagus regained its power the pulse became slow with an occasional quick beat interpolated (Fig. 95), and finally the pulse became slow and regular (Fig. 98); the

FIG. 94.—Pulse tracing from a case of poisoning by digitalis, showing quick pulse with slow beats interposed.

FIG. 95.—Same case.—Recovering from the effects of the poison, and showing slow pulse with occasional quick beats.

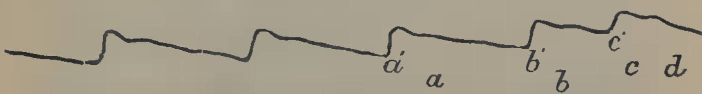


FIG. 96.—Same case.—Slow pulse, with beat interpolated at *b*.

FIG. 97.—Same case.—Pulse regular, but quickened by food.

FIG. 98.—Same case.—Recovering; pulse slow and regular.

slowness of the pulse is probably due to the vagus causing a certain degree of heart-block (Fig. 50, p. 145).

Action of Digitalis on the Kidneys.—It has already been mentioned that the vaso-motor centre has the function of distributing blood to different parts of the body, so that while one

contracts another dilates. In consequence of this very great differences indeed may occur in the circulation in different parts of the body without any alteration in the general blood-pressure. This appears to be the case with

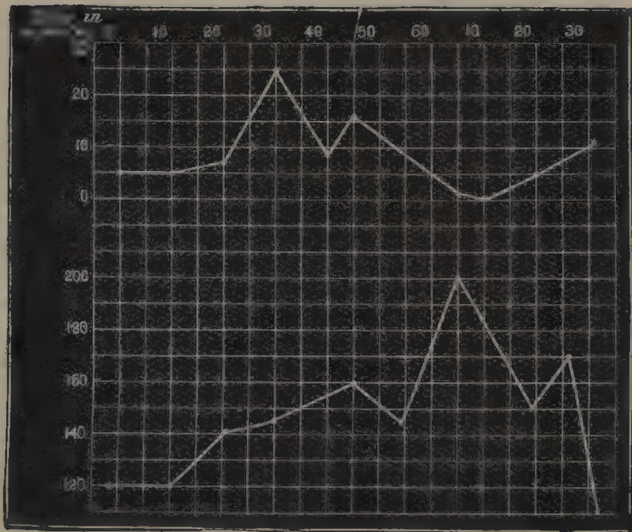


FIG. 99.—Diagram to show the relation between blood-pressure and the secretion of urine after the administration of erythrophlœum. The lower tracing shows the blood-pressure in millimetres of mercury. The upper shows the secretion of urine in minims per ten minutes. It is to be noted that when the blood-pressure rises to its maximum of 200, the secretion of urine falls to zero. (Brunton and Pye.)

digitalis, which tends to contract the vessels in the splanchnic area and at the same time, or even before this, to dilate those of the kidney.[16] If the circulation through this organ is very greatly increased the pressure upon the glomeruli rises and the urine is secreted

much more quickly. This abundant secretion may occur without any rise in blood-pressure. When the digitalis is exerting its full action upon the arterioles so that the pressure rises very much, the drug instead of increasing the secretion of urine may stop it altogether, producing in fact the same effect as ligature of the renal artery. When this contracting effect of digitalis begins to pass off the vessels of the kidney again dilate and the secretion again becomes abundant, just as it would if the ligature had been removed from the arteries of the kidney previously ligatured.[17] The same effect is produced by other drugs of the digitalis group, such as erythrophlœum (Fig. 99).[18]

Résumé of the Action of Digitalis.—Digitalis acts on the cardiac muscle, the intrinsic cardiac nerves, and the vagus centre in the medulla. It also affects the arterioles, causing them to contract, and probably it has upon them also a twofold action, as on the heart, stimulating both the contractile muscular walls and the nerves which go to them. From stimulation of the vagus centre[20] the pulse becomes slow, and the diastole more complete,[21] while at the same time the stimulation of the muscular fibre of the heart makes its contractions more powerful.[22] Its beats thus become much more efficient; the longer intervals between them afford the heart time for recuperation; the more complete diastole allows a larger quantity of blood to accumulate in its cavities, the more powerful systole drives this onward, so that under the influence of digitalis each cardiac contraction

may do from two and a half to three and a half times what it did before.[23] The self-massage of the heart becomes more complete (p. 154), and all the good effects which I have mentioned as occurring from this are noticed after the action of digitalis. One consequence which is of special interest is its diuretic action. This is partly due to the rise in blood-pressure which it produces, and which raises the pressure in the glomeruli, drives the blood more quickly through the kidneys, and causes a more rapid secretion of urine. At the same time it is probable that digitalis has a certain stimulating effect on the secreting structures in the kidneys themselves, a stimulation which may extend also to other parts of the genito-urinary tract. This effect, however, is not so great as that produced by caffeine, and the diuretic action of digitalis is probably exerted chiefly through the circulation. When digitalis acts upon a healthy man so as to produce diuresis, the drain of fluid becomes so great that, as I have found in my own experiments, the thirst it induces becomes intolerable, and water must be taken in order to allay it.[19]

In cardiac diseases with œdema, or accumulation of fluid in the serous cavities, such drinking is unnecessary, as the fluid drained away from the blood by the kidneys is supplied by absorption from the subcutaneous tissues or from the serous cavities.

Uses of Digitalis.—Not only does the circulation in the tissues generally improve under digitalis, but the nutrition of the heart is

increased by more efficient circulation through the coronary vessels, dilatation is lessened, the muscular rings around the auriculo-ventricular orifices contract more strongly, the mitral and tricuspid valves close them more efficiently, and regurgitation is lessened. In cases where the valvular incompetency is solely due to dilatation and not to changes in the valves themselves, the incompetency may be completely cured (p. 75).

The arteries likewise benefit, as the slower and stronger beats of the heart increase the self-massage of the artery in its sheath (p. 156), and the same increased pulsation aids the circulation in the veins, as already described. The venous circulation is further aided by increased suction power of the heart (p. 154), which contracts more rapidly and completely. Diminished regurgitation combines with increased circulation in the veins to lessen venous congestion, and thus tends to increase the secretion of urine. For venous congestion in the kidneys tends to compress the arterioles and tubules in the organ, and thus lessen secretion; and digitalis, therefore, in cases of venous congestion probably acts as a diuretic in four ways—(1) it dilates the renal vessels and increases the blood-pressure in the glomeruli; (2) it lessens the resistance which the pressure of the distended venous radicles in the kidney opposes to secretion; (3) it probably acts as a stimulant to the secreting cells of the kidney; and (4) it increases the volume of blood, and somewhat alters its composition by causing absorption from

œdematous tissues and serous cavities. When it causes absorption of ascitic fluid from the abdominal cavity it may act as a diuretic in a fifth way, viz., by lessening the resistance opposed to the secretion of urine by the pressure of the ascitic fluid on (*a*) the kidney itself, and (*b*) on the ureters. From this manifold action of digitalis as a diuretic it is evident that when its action is once fairly established in a water-logged patient, the amount of urine secreted for some days may be enormous.

Action of Digitalis on Œdema.—As I have already mentioned, the diuretic action of digitalis may cause so much water to be withdrawn from the blood that it produces a consuming thirst in a healthy man.[24] In a dropsical one, the fluid lost through the kidneys is made up by absorption from the tissues, and this is one way in which digitalis reduces œdema. But it is probably not the only one. For digitalis stimulates the vasomotor nerves, and in this way tends to prevent the exudation of fluid from the blood-vessels, which produces œdema. It is universally acknowledged that venous obstruction tends to produce œdema, but at the same time œdema may occur without any obvious venous obstruction, as in angioneurotic œdema. Moreover, venous obstruction may exist without œdema, as was shown by Ranvier,[25] who tied the vena cava in a dog, and found that although venous congestion was thus produced in both legs, no œdema occurred in the leg where the

vaso-motor nerves were left intact, but occurred in the other where the vaso-motor nerves were divided.

Another benefit resulting from diminished venous congestion is improved digestion and assimilation. The liver, which under increased venous pressure may have become so swollen as to reach even below the umbilicus, returns more or less to its normal size, and the obstacle which had existed to the return of venous blood from the stomach and intestines, nearly all of which has to pass through the liver, is removed. The circulation through these organs becomes better, digestion and absorption improve, flatulence is lessened, and the patient's nutrition improves.

Congeners of Digitalis. — Digitalis is an example of a very widely distributed group of poisons, many of which are used in various parts of the world for poisoning arrows, either for use in the chase or in war. Those which are most commonly used in medicine are the *Strophanthus hispidus* and squill (*Urginea Scilla*). Amongst those occasionally, but less frequently, employed are casca or sassy bark (*Erythrophlœum guineense*), lily of the valley (*Convallaria majalis*), Canadian hemp (*Apocynum cannabinum*), pheasant's eye (*Adonis vernalis*), Christmas rose (*Helleborus niger*), and Cactus grandiflora. Other plants having a similar action, but not used, are *Antiaris toxicaria* (upas), *Nerium oleander*, *Acocanthera* (oubain), *Thevetia grandiflora*, *Tanghenia venenifera*, and *Coronilla*. A poison having a similar action is

obtained from the skin of toads.[26] It is called phrynin, and though not employed much in medicine, it has proved useful. The story is told that the husband of an Italian woman was dying of heart disease, with dropsical limbs and all the usual accompaniments. As his death was so slow, his goodwife thought she would quicken his journey into the other world, and accordingly she went into the garden, where she found several toads. These she dropped into the wine her husband was to drink; but instead of his dying forthwith, as she expected, he began immediately to get well, the phrynin from the toads' skin having had upon him the same beneficial effect that a course of digitalis would have had.

Difference between Digitalis and other Cardiac Tonics.—The differences which have been observed between the action of digitalis and its congeners are that, while digitalis affects both heart and vessels,[27] the action of strophanthus appears to be exerted more especially upon the heart,[28] increasing its power; while that of erythrophlœum appears to be exerted more upon the vessels.[29]

Drawbacks to the Action of Digitalis and other Cardiac Tonics.—All the drugs of which we have hitherto been speaking have a tendency to cause contraction of the vessels. This tendency may interfere with their beneficial effects by causing contraction of the renal arteries, and thus checking the secretion of urine; but a greater drawback sometimes is that, by contracting the vessels generally, they

raise the blood-pressure and thus increase the resistance which the heart has to overcome, and consequently the work it has to do. If the heart is very feeble, it may even become unable to overcome the increased tension, and sudden and fatal syncope may ensue. Fatal syncope has not infrequently resulted from the excessive use of digitalis, and it appears to be more apt to come on when the person rises to micturate. The sudden change from a recumbent to an upright position lessens the pressure of blood in the cerebral arteries, while, at the same time, by emptying the bladder the intra-abdominal pressure is lessened, and the blood is retained in the splanchnic area. But the cases in which the heart is most likely to be stopped by digitalis are those in which the arterial pressure is already high, as in advanced Bright's disease, and where the heart has already become fatty. In such cases digitalis must be used with great caution, for there is a double risk. On the one hand there is the danger just alluded to of stopping the heart, and on the other, there is the risk of causing apoplexy by the arterial tension rising so high as to burst a vessel in the brain.

Removal of these Drawbacks by Combination.—Yet in many such cases we sadly want the steadying and strengthening effect of digitalis or strophanthus upon the heart, and we are able to obtain the result we desire by combining these drugs with others belonging to an entirely different class, namely, that of vaso-dilators.

Digitalis in Cases of Fatty Heart.—In my thesis, presented to the University of Edinburgh in 1866, I closed the part on the use of digitalis with the following remarks. "With just one word of warning, I will close this brief summary of the therapeutical applications of digitalis, and that is to those who, thinking that there can be no danger in giving digitalis to those with very weak hearts, and that indeed it is the best thing for them to use it indiscriminately. I believe that I have proved that it increases the force of the cardiac pulsations; but if, while the motor nerves were stimulating it to contract, and the capillaries at the same time were opposing a resistance, the fibres of the heart itself were not composed of sound muscle, but were fatty and friable, some of them would be pretty sure to rupture, and the results would be disastrous. I therefore think that, in cases of fatty heart, great caution is necessary in administering it."[30] This warning has received remarkable confirmation within the last few months, as Scalfati[31] has found that in dogs whose hearts he had rendered fatty by means of phosphorus the effects produced by digalen, digitalin, digitoxin and strophanthin were in more or less strict relation to the amount of fatty degeneration present. When this was slight the effect was much the same as in a normal heart, but if the heart was much degenerated the effects of the digitalis group were very temporary, and were soon followed by a period of depression and cardiac inefficiency.

Action of Adrenalin on the Heart and Vessels.—This substance when injected into the circulation causes a rise of blood-pressure, such as almost no other substance, except nicotine, p. 323, will produce.[32] This is due to its action both on the heart and vessels. It appears to stimulate the post-ganglionic terminal branches of sympathetic nerves[33] throughout the whole body, dilating the pupil,[34] increasing saliva and tears,[35] contracting the uterus,[36] but inhibiting the intestine,[37] stomach, bladder, and sphincters[38] by an action on the splanchnic.[39] It causes contraction of all the arterioles in the body[40] with the exception of the coronary arteries, and these it dilates.[41] It causes the heart to beat more strongly and also more quickly,[42] unless at first, when the rise in arterial pressure which it produces may stimulate the vagus roots and thus slow the pulse.[43]

In cases of shock or collapse it is one of the most powerful remedies we possess when injected into a vein or even subcutaneously;[44] a disadvantage it possesses is that its action is very temporary. This may possibly be connected with a curious point in relation to its chemical constitution and physiological action. The adrenalin from suprarenal capsules is lævo-rotary, whilst the synthetic adrenalin consists of an admixture of two kinds of adrenalin, one of which is lævo- and the other dextro-rotary. The synthetic lævo-adrenalin acts like that from suprarenal capsules. The dextro-adrenalin has hardly any physiological action,[45] but it has the power of preventing the action of lævo-adrenalin

when subsequently administered even in large doses[46] (*cf.* Muscarine, p. 280).

When given by the mouth adrenalin is comparatively feeble.

Camphor.—Camphor is an exceedingly powerful stimulant both to the heart and to the vessels. When applied to the frog's heart it increases the frequency and power of its contractions,[47] and when the heart has been brought to a complete standstill by muscarine, small quantities of camphor added to the nutrient solution will produce occasional pulsations.[48] When the heart has been poisoned by chloral and is beating very slowly and very feebly, camphor increases both the frequency and power of the contractions.[49] It stimulates the vaso-motor centre in the medulla and produces contraction of the blood-vessels[50] so as to raise the blood-pressure, even when it has been greatly lowered by chloral.[51]

The most remarkable action of camphor, however, is its power to stop fibrillation of the heart (p. 62) when excised,[52] and possibly also when in the body.[53] It was at one time very largely used, though of late years it has fallen out of fashion. It was regarded by Pereira as a vascular excitant.[54]

Action of Strychnine on the Heart.—Another drug most useful in cardiac disease is strychnine. Its action is exerted slightly, if at all, upon the muscular fibre, but it greatly increases the reflex excitability of nerve centres. This is more especially marked in those of the cord and medulla, such as the vaso-motor centre, but

it also stimulates peripheral ganglia, and Cash and I found that when applied to the heart it prevented the slowing or stoppage of the ventricle, which usually occurs from the application of a ligature between the venous sinus and the ventricle (p. 269).[55] In some books on Pharmacology the action of strychnine as a cardiac stimulant is to a great extent ignored; but I think that in medical practice the use of this drug as a cardiac stimulant has of late years become more and more general, and it is justified by the good effects observed from it, and explained, partly at least, by the action on the heart which Cash and I found it to have. Under its use we frequently notice that a pulse which was previously feeble, irregular, or intermittent, becomes steady, strong, and regular. No doubt the conditions which regulate the pulse are very complicated in health, and still more in disease, so that it is difficult or impossible to be absolutely certain of the exact mode of action of strychnine; but at the same time its good effects are, I think, undeniable, and the explanation that I have given is at any rate feasible.

Action of Caffeine and other Purin Bodies.—While strychnine exerts its beneficial effect almost entirely through the nerves, caffeine and allied bodies probably exert it more especially through their stimulating action upon the muscular fibres or peripheral nervous system of the heart,[56] and upon the secreting cells[57] in the kidneys. This is not entirely the case, however, for all the plants which contain either caffeine or theobromine are used dietetically as stimu-

lants to the nervous system: tea, coffee, and chocolate being the most commonly employed, but kola and guarana being also largely used in Africa and South America. Like digitalis, caffeine stimulates the vaso-motor centre in the medulla[58] and raises the blood-pressure by causing contraction of the vessels. This rise is sometimes accompanied by a slow pulse, as in the case of digitalis, from stimulation of the vagus centre.[59] Usually, however, it goes along with an acceleration of the heart-beats. The reason of this probably is that the cardiac muscle or its contained nerves are rendered by caffeine more irritable,[60] and the coronary arteries dilate,[61] so that the rhythmical stimuli follow one another more quickly. The effect upon the kidneys is to produce a considerably increased flow of urine, and the increase of water is accompanied also by an increase in the solids,[62] the total effect being chiefly due to stimulation of the secreting cells, although along with this there is dilatation of the renal vessels also.[63] Theobromine differs from caffeine in having much less effect upon the vaso-motor centre and more effect upon the kidney itself.[64] It therefore acts more powerfully as a diuretic than caffeine. It is sparingly soluble in water, but is rendered more soluble by trisodium phosphate, and several synthetic compounds have been introduced into medicine. One is called diuretin,[65] which is said to be a salicylate of sodium and theobromine; agurin, which is an acetate of sodium and theobromine; an iodide of sodium and theobromine; and uropherin,

which is a salicylate of lithium and theobromine. Synthetical theophyllin is sold under the name theocine. All these substances are useful diuretics, and may be given alone or in combination with digitalis, strophanthus, or drugs having a similar action. When digitalis or other substances of that group fail to act, a combination of them with one of the diuretics group may succeed.

Pituitary Gland.—An extract of the posterior part of the gland causes vascular contraction, rise of blood-pressure, and increased power of cardiac contractions. It differs from adrenalin in the more prolonged rise of blood-pressure, and in slowing the heart whether the vagus is intact or divided, thus it is an exceedingly powerful stimulant in depressed circulatory conditions, and has almost miraculous results in veronal poisoning after strychnine has failed. It dilates the kidney vessels and greatly increases the urine, hence it is useful in suppression of urine. If a second dose is given within an hour or two after the first, its effect is lessened or abolished, except that the second dose, while failing to raise the blood-pressure, still increases the urine. This diuretic action would seem to be partly due to a specific action on the kidney secretory cells. It also causes powerful contraction of the uterus, which renders it of service in post-partum hæmorrhage, and of the intestine, whence it may relieve post-operative intestinal paralysis and lessen hæmorrhage in typhoid fever. To obtain a rapid action in the cases mentioned, the extract should be injected into the muscles, and

in severe shock it should be given intravenously. In chronic cases of cardiac debility and dilatation it may be given by the mouth.[66]

LITERATURE.

[1] James Blake, *Edin. Med. and Surg. Journ.*, 1839, vol. li., p. 342.

[2] L. Traube, *All. med. Centr.-Ztg.*, 30th Jahrg., 1861; and *Gesammelte Beiträge*, 1871, vol. i., p. 277.

[3] L. Traube, *Centralb. f. d. med. Wiss.*, p. 885, 1865.

[4] L. Traube, *Berlin klin. Wochenschr.*, 1871.

[5] Lauder Brunton, *On Digitalis*, 1866; reprinted in *Collected Papers*, First Series (London: Macmillan & Co. Ltd., 1907).

[6] Schmiedeberg, *Beiträge zur Physiologie Festschr. für C. Ludwig*, p. 224, 1874.

[7] Fagge and Stevenson, *Roy. Soc. Proc.*, 1865, vol. xiv., p. 273.

[8] Pickering, *Journ. of Physiol.*, 1893, vol. xiv., p. 383.

[9] Pickering, *op. cit.*, p. 436.

[10] Brunton and Cash, *St Barth. Hosp. Rep.*, 1882, p. 267.

[11] K. Hedbom, *Skand. Arch. f. Physiol.*, vol. viii., pp. 147, 169; *Centralb. f. Physiol.*, 1898, Bd xii., p. 364.

[12] Brunton and Meyer, *Journ. of Anat. and Physiol.*, vol. vii., 1873, p. 134; reprinted *Collected Papers*, p. 141.

[13] Lauder Brunton and Tunnicliffe, *Journ. of Physiol.*, 1896, vol. xx., p. 354.

[14] Brunton and Power, *Centralb. f. d. med. Wiss.*, 1874, p. 497; and *Proc. Roy. Soc.*, 1874, vol. xxii., p. 420.

[15] Brunton and Pye, *Proc. Roy. Soc.*, 1876, vol. xxv., p. 172; *St Bartholomew's Hospital Reports*, 1876, vol. xii., p. 125; *Phil. Trans.*, 1878, vol. clxvii., part ii., p. 627.

[16] Loewi, *Wiener klin. Wochenschr.*, 1907.

[17] Brunton and Power, *op. cit.*

[18] Brunton and Pye, *op. cit.*

[19] Lauder Brunton on "Digitalis," *Collected Papers*, p. 83 (Macmillan & Co.: London, 1906).

[20] Ackermann, *Deutsch. Arch. f. klin, Med.*, 1873, vol. xi., p. 125; Kochmann, *Arch. de Pharmacodynamie et de Therap.*, 1905, vol. xvi., p. 221 *et seq.*

[21] Braun and Mager, *Sitzungsb. d. Wiener Akad.*, 1899, vol. cviii., p. 741 *et seq.*
[22] Gottlieb, Meyer and Gottlieb's *Pharmakologie*, p. 224.
[23] Gottlieb and Magnus, *Arch. f. exp. Path. u. Pharm.*, 1904, vol. li., p. 63.
[24] Lauder Brunton on "Digitalis," Notes of 17th and 19th March 1865, *Collected Papers on Circulation and Respiration*, p. 83.
[25] Ranvier, *Compt. rend.*, 1869, vol. lxix., p. 1326; Hehn, *Centralb. f. d. med. Wiss.*, 1873, p. 625; Janowski, 1883, *Virch. Arch.*, vol. xciii., p. 259.
[26] For the action and literature of most of these, *vide* Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, 1883, vol. xvi., p. 149 *et seq.*
[27] Brunton, *op. cit.*
[28] T. R. Fraser, *Journ. of Anat. and Physiol.*, 1885, vol. vii., p. 154.
[29] Brunton and Pye, *op. cit.*
[30] Brunton on "Digitalis," etc., 1868 (London: Churchill), p. 58; and *Collected Reprints*, First Series, 1907, p. 77.
[31] Scalfati, *Rif. med.*, 6th April 1911; abstracted in the *Brit. Med. Journ. Epitome*, 14th Sept. 1912, p. 36.
[32] Oliver and Schäfer, *Journ. of Physiol.*, 1895, vol. xviii., p. 239, giving earlier literature.
[33] Langley, *Journ. of Physiol.*, 1901-2, vol. xxvii., p. 256, and 1905-6, vol. xxxiii., p. 405; Elliot, *ibid.*, 1905, vol. xxxii., p. 429.
[34] Lewandowsky, *Arch. f. Anat. u. Physiol.*, 1899, p. 360; Boruttau, *Pflüger's Arch.*, 1899, vol. lxxviii., p. 112; Langley, *Journ. Physiol.*, vol. xxvii., p. 244.
[35] Langley, *op. cit.*, vol. xxvii., pp. 238 and 247.
[36] Langley, *op. cit.*, vol. xxvii., p. 252.
[37] Boruttau, *Pflüger's Arch.*, 1899, vol. lxxviii., p. 113; Langley, *op. cit.*, vol. xxvii., p. 249.
[38] Langley, *op. cit.*, vol. xxvii., p. 255.
[39] Pflüger, *Ueber d. Hemmungsnervensystem f. d. peristaltische Bewegungen d. Gedärme* (Berlin, 1857).
[40] Oliver and Schäfer, *op. cit.*, vol. xviii., p. 239.
[41] Douglas Cow, *Journ. of Physiol.*, 1911, vol. xlii., p. 132.
[42] Gottlieb, *Arch. f. exp. Path. u. Pharm.*, 1897, vol. xxxviii., p. 99; and 1899, vol. xliii., p. 286.
[43] Oliver and Schäfer, *op. cit.*, vol. xviii., p. 247.

[44] Crile, *Blood Pressure in Surgery*, pp. 412 and 413 (Philadelphia and London : Lippincott Co., 1903).
[45] Cushny, *Journ. of Physiol.*, 1908, vol. xxxvii., p. 130 *et seq.*
[46] Fröhlich, *Centralb. f. Physiol.*, 1909, vol. xxiii., p. 254.
[47] Heubner, *Arch. f. Heilk.*, 1870, vol. ix., p. 334 ; Baum, *Centralb. f. d. med. Wiss.*, 1870, vol. viii., p. 467.
[48] Harnack and Witkowski, *Arch. f. exp. Path. u. Pharm.*, 1876, vol. v., p. 429 ; Wiedemann, *ibid.*, 1877, vol. vi., p. 222.
[49] Gottlieb, Meyer and Gottlieb, *Pharmakologie*, p. 216.
[50] Wiedemann, *Arch. f. exp. Path. u. Pharm.*, 1877, vol. vi., p. 227.
[51] Alexander-Lewin, *ibid.*, 1890, vol. xxvii., p. 231 ; Bohme, *ibid.*, 1905, vol. lii., p. 346 *et seq.*
[52] Seligmann, *Arch. f. exp. Path. u. Pharm.*, 1905, vol. lii., p. 341.
[53] Seligmann, *op. cit.*, p. 345.
[54] Pereira, *Elements of Materia Medica and Therapeutics*, 4th ed., vol. ii., part i., p. 454 (London : 1855).
[55] Brunton and Cash, "On the Explanation of Stannius's Experiment, and on the Action of Strychnia on the Heart," *St Bartholomew's Hospital Reports*, vol. xvi., 1880 ; in *Collected Papers*, p. 557 ; *cf.* p. 558.
[56] Dreser, *Arch. f. exp. Path. u. Pharm.*, 1888, vol. xxiv., p. 240 ; Bock, *ibid.*, 1900, vol. xliii., pp. 387 and 398.
[57] von Schroeder, *Arch. f. exp. Path. u. Pharm.*, 1897, vol. xxii., p. 57.
[58] Bock, *op. cit.*, pp. 390 and 399.
[59] Bock, *op. cit.*, p. 398.
[60] Bock, *op. cit.*, p. 398.
[61] Hedbom, quoted by Bock, *op. cit.*, pp. 368 and 392.
[62] von Schroeder, *op. cit.*, vol. xxii., p. 47.
[63] Loewi, *Wien. klin. Wochensch.*, 1907, No. 1.
[64] von Schroeder, *op. cit.*, vol. xxiv., p. 101.
[65] Hoffmann, *Arch. f. exp. Path. u. Pharm.*, 1891, vol. xxviii., p. 1 *et seq.*
[66] Schäfer, *Pharmaceutical Journ.*, 1907, vol. lxxix., p. 670 ; *ibid.*, *Roy. Soc. Proc.*, 1909, B, vol. lxxxi.

CHAPTER XIII

ACTION OF CARDIAC DEPRESSANTS

Nicotine — Tobacco-Smoking — Effects of Smoking — Attractions of Smoking — Excessive Smoking — Aconite.

Nicotine.—Another drug which has a very powerful influence upon the blood-pressure and cardiac action is nicotine. Both in frogs and mammals nicotine produces, first convulsions and then paralysis.[1] When applied in small doses to the frog's heart, it causes the beats at first to become slow and afterwards quick.[2] If the dose be large, no primary slowing may be observed. In animals it causes slowing of the heart, with enormous rise of blood-pressure.[3] The rise of blood-pressure is so great that I have never seen it equalled after the injection of any drug, with the exception of suprarenal extract. The rise of pressure is chiefly due to contraction of the arterioles. This contraction is partly dependent upon stimulation of the vaso-motor centre in the medulla oblongata, but partly also to a local action upon the arterioles themselves, as it may be produced by injection of the drug even after

the medulla has been destroyed. The pulse-rate in mammals is first slowed and afterwards quickened, just as in the frog. The slowing is due partly to stimulation of the vagus centre in the medulla oblongata, and partly to the stimulation of the inhibitory apparatus in the heart itself. The subsequent increase in the pulse-rate is due to paralysis of these ganglia. In consequence of this double action of nicotine, if the vagus be divided during the period of slow pulse, the pulse becomes somewhat quicker, but still remains slower than normal. When, however, the dose has been sufficiently large to quicken the pulse, no stimulation of the vagus will slow the heart, as its terminal branches in the heart are paralysed by the drug.[5] This action is the same in the heart of the frog, so that after a large dose of nicotine, stimulation of the vagus has no effect upon the heart, but stimulation of the venous sinus itself will slow the heart.[6] The reason of this probably is, that although the inhibitory ganglia in the heart are paralysed, the inhibitory neurons which proceed from them are still intact, and are affected by local stimulation.[7]

Formerly tobacco enemata were used as a means of causing vascular and general relaxation, but they were far from being without danger and are never employed now.[8] But although tobacco is not used as a remedy for disease, its employment is so universal that its action requires very careful consideration. Nicotine alone is only taken into the body

when tobacco is used by chewing or by snuffing. When it is chewed, most of the juice is expectorated, but a small portion is probably swallowed. When tobacco is used in the form of snuff, small quantities of it find their way into the naso-pharynx and they are swallowed. The tobacco used for chewing or snuffing contains, as a rule, but very little nicotine, and so symptoms of poisoning from either of those habits are rare.

Tobacco-smoking.—Usually tobacco is employed by smoking, either in the form of cigars or cigarettes, or in a pipe. When used in any one of these forms it is not pure nicotine which reaches the mouth, but really the products of the dry distillation of tobacco, containing a large quantity of pyridine and picoline bases. Probably nicotine in greater or less quantity is also present.[9] The proportions of the pyridine and picoline bases in the tobacco-smoke vary according to the mode in which it is burnt. In a cigar there is a freer access of air, so that much collidine and little pyridine are formed, while in a pipe much more pyridine is produced, and thus stronger tobacco can be smoked in a cigar than in a pipe. So much is this the case, that tobacco which in the form of a cigar would produce no disagreeable effect may cause giddiness and vomiting if smoked in a pipe.[10] The smoke from a pipe or cigar usually passes simply into the mouth and out again, either through the mouth or the nostrils; but when smoked in a huka or narghileh, the smoke is inhaled into the lungs,

and this is frequently done also by people who smoke cigarettes. When a huka or a narghileh is used, the smoke passes through water before being inhaled, and it is thus deprived of most of its poisonous constituents; but this is not so with the smoke of cigarettes, and as absorption occurs very rapidly from the pulmonary mucous membrane, cigarette-smoking is sometimes very injurious. There is another reason, however, why cigarette-smoking is frequently more harmful than smoking a pipe or cigar, and it is that cigarettes are small and can be smoked in a few minutes, so that many more cigarettes than pipes or cigars are consumed in the course of the day, and the total quantity of tobacco used is thus much greater in the form of cigarettes.

Smoking in moderation does not seem to be injurious to grown-up people, but there appears to be a general consensus of opinion that it is very distinctly harmful to growing lads.

Attractions of Smoking.—In adults, smoking appears to have a double action. It will stimulate the brain to increased activity, and it will also produce a soothing effect in conditions of excitement. Its stimulating effect upon mental activity is probably partly due to the local irritant action of smoke upon the mouth, causing reflex dilation of the vessels which supply the brain in somewhat the same way as mastication.[11] Its action as a sedative is probably partly due to the necessity of breathing rhythmically while smoking, and the soothing effect of watching the smoke as it issues from the lips or nostrils,

especially when it is blown out in the form of rings. This is by no means an unimportant factor, for many people derive but very little pleasure from smoking in the dark.

Results of Excessive Smoking.—One of the commonest results of excessive smoking is chronic pharyngitis, with irritability of the throat, cough and hoarseness, and sometimes the irritation also affects the tongue. Weakness of vision, nervous tremor, and giddiness frequently result from tobacco-smoking. It is difficult to decide how far these are due to the direct action of the tobacco-smoke upon the nervous system and how far they are caused through alteration in the circulation. The circulation becomes much affected; palpitation and pain in the cardiac region are common results. Sometimes, though rarely, the cardiac pain may be so great as to simulate angina pectoris. Irregularity of the heart is very common, and it appears to me that this irregularity is more frequently found from a common kind of tobacco known as "pigtail" than from better-class tobaccos. When I was a house physician I met with it very frequently, and the cardiac rhythm might be represented somewhat in this way:  a pause, followed by one or two heavy beats, then a succession of quick, small beats, and then a pause again. With better-class tobaccos I have not observed this irregularity so frequently, but I have more often seen the patient simply fall

down unconscious, as if he had been shot. These unpleasant symptoms, as well as the nervous symptoms which accompany them, may sometimes cease upon lessening the amount of tobacco used, but not unfrequently a very small quantity appears to keep up the condition after it has once been established; and complete abstinence from tobacco, occasionally for a period of several months, is required before it can be resumed without causing a recurrence of the symptoms. I have found that a very low arterial tension, 90 to 110, or even lower in persons otherwise healthy, is frequently an indication of excessive smoking, *cf.* p. 181.

Aconite.—Aconite [12] is a drug which may be looked upon as a typical cardiac depressant. Its most characteristic physiological action is that of causing numbness and tingling when applied to the tongue in small quantities, and this test is much more delicate than any chemical reaction. When administered to mammals in small doses it slows the heart very greatly, and this effect is entirely due to its action upon the vagus centre. Its effects are precisely similar to those produced by stimulation of the vagus, the heart being rendered slow and the blood-pressure failing. In larger doses it paralyses the ends of the vagus in the heart, so that the pulse becomes suddenly very rapid and at the same time very irregular, while the blood-pressure oscillates in a remarkable manner.[13] It appears to have also a local action on the cardiac muscle, but this is of a very complex nature,[14] and, I think, is

probably connected with stimulation and paralysis of some sensory mechanism in the heart itself, to which the cardiac pulsations are partly due. That such a reflex mechanism actually exists in the heart itself appears to be shown, amongst other things, by the experiments of von Basch and A. Fröhlich[15] upon the action of cocaine on the heart. They found that when the surface of the heart was stimulated by a faradic current, which caused an extra beat and compensatory pause, this effect diminished rapidly when cocaine was applied to the surface of the heart. This action was not due to any effect of cocaine upon the cardiac muscle, but only to its local action on the epicardium. It is not improbable that the effect of aconite upon the heart may be due to an action upon the sensory mechanism in it somewhat analogous to that of cocaine. One effect of aconite is to disturb the rhythm very greatly, so that in the frog's heart the normal beats and peristaltic action may alternate.

The chief use of aconite is in local inflammations accompanied by general febrile disturbance. Small doses of this drug appear occasionally to be exceedingly useful, for example, in tonsillitis and in febrile colds.[16] In nervous flutterings of the heart, aconite in small doses appears to quiet the circulation, but how it does so I cannot at present explain. Very small doses are sufficient, and often seem to slow the pulse more than larger ones. One minim of the pharmacopœial tincture every hour is frequently sufficient, although

the dose given in the *British Pharmacopœia* is 2 to 5 minims, frequently repeated, or 5 to 15 minims when given at longer intervals. In cases of persistent high tension with attacks of angina pectoris, aconite is sometimes useful. Its action should be regulated by a sphygmomanometer.

LITERATURE.

[1] Van Praag, *Virchow's Archiv*, vol. viii., p. 56; Wachenfeld, quoted by Husemann, *Pflanzenstoffe*, 2nd ed., p. 1174 (Berlin: Springer, 1882).

[2] Schmiedeberg, *Sitzungsb. d. k. sächs. Gesellsch. d. Wiss.*, 1870, p. 130 *et seq.*; and *Ludwig's Arbeiten*, 1870, p. 41 *et seq.*

[3] L. Traube, *All. med. Centr.*-, 1862; and *Gesam. Beiträge*, 1871, vol. i., p. 302 (Berlin: Hirschwald). For other literature, see Kobert, *Lehrb. d. Intoxikationen*, 2nd ed., Bd. ii., p. 1069 (Stuttgart: Enke, 1906).

[4] Rosenthal, *Centralb. f. d. med. Wiss.*, 1863, p. 736.

[5] Rosenthal, *op. cit.*

[6] Schmiedeberg, *op. cit.*

[7] Langley and Dickinson, *Journ. of Physiol.*, 1890, vol. xi., p. 265.

[8] Pereira, *Materia Medica*, vol. ii., part i., p. 583, 4th ed. (London: Longmans, 1855).

[9] See literature in Kunkel's *Handb. d. Toxicologie*, p. 681 (Jena: Fischer, 1901).

[10] Vohl and Eulenburg, *Arch. Pharm.*, vol. ii., part cxlvii., pp. 130-166; abstracted by Lauder Brunton in *Journ. Chem. Soc.*, 1871, New Series, vol. ix., p. 1075.

[11] Marey, *Circul. du Sang*, p. 319 (Paris: Masson, 1881).

[12] For literature, *vide* Husemann, *Pflanzenstoffe*, 2nd ed., vol. i., p. 624 (Berlin: Springer, 1882); and Kobert, *Lehrb. d. Intoxikationen*, 2nd ed., Bd. ii., p. 1147 (Stuttgart: Enke, 1906).

[13] Cash and Dunstan, *Roy. Soc. Proc.*, 1898, vol. lxii.,

p. 341; *vide* also, *Roy. Soc. Proc.*, 1901, vol. lxviii., pp. 378 and 384.

14 Schmiedeberg, *Grundriss d. Pharmakologie*, p. 163 (Leipzig: Vogel, 1902).

15 von Basch and A. Fröhlich, *Centralb. f. Physiol.*, Bd. xviii., Literatur, 1904, p. 693.

16 Ringer and Sainsbury, *Handbook of Therapeutics*, 13th ed., p. 470 (London: Lewis, 1897).

CHAPTER XIV

ACTION OF DRUGS ON BLOOD-VESSELS

Drugs acting on the Blood-vessels—Vaso-motor Contractors—Peripheral and Central—Vaso-dilators—History of their Discovery—Classes of Vaso-dilators—Iodides—Effect of Drugs upon the Coronary Arteries.

Action of Drugs upon the Blood-vessels.—The blood-vessels may be either dilated or contracted by the action of drugs, and these effects may be produced either by central or peripheral action. These actions may either aid one another, as in the case of nitrite of amyl already cited, or may tend to counteract one another. I have already mentioned that the vaso-motor centre has the function of regulating the distribution of blood in the body, so that when the vessels in one district are dilated, those in another are contracted. Thus very great variations may occur in the local distribution of blood without any alteration in the general blood-pressure, although when many vessels contract at the same time the pressure will rise, and when many are dilated the pressure will fall. The selective action of drugs is very well marked in regard to the blood-vessels, so

that not only may the vessels which supply one vascular area be contracted while others are dilated by a certain drug, but the same parts of the vessel in one vascular area may be contracted while others are dilated. As the splanchnic area is the most powerful in regulating blood-pressure (p. 19), one would naturally expect that its vessels would react more quickly to drugs than those of other parts, and accordingly it has been found that whilst adrenalin causes very marked contraction in the splanchnic arteries it has less action upon those of the legs, and produces dilatation instead of contraction in the coronary arteries.[1] Whilst the splanchnic vessels are contracted on the whole by adrenalin it does not act equally upon the whole of them because some parts may be actually dilated by it while other parts are contracted (*cf.* p. 315).

Vaso-motor Contractors. Peripheral. — As the local contraction of vessels is the means by which the supply of nutriment and oxygen to the tissues is regulated, the amount of oxygen contained in the blood has a powerful action on the size of the vessels. As Ludwig [2] has pointed out, when the blood supplied to an isolated organ is richly arterialised, the vessels contract, and the circulation through it becomes lessened. If the supply of blood be stopped so that the tissues become, as it were, asphyxiated, the vessels dilate and the circulation becomes exceedingly rapid when it is again re-established; just as when a man ceases to breathe for a few moments he is obliged to take several deep breaths immediately afterwards.

Reaction of the circulating fluid is of great importance, as acids tend to cause dilatation and alkalies contraction.[3] The effect of alkaline bases on the vessels is not always the same as upon the heart, for potash salts, as already mentioned, tend to cause enfeeblement of the heart with stoppage in diastole, while they have an opposite effect on the vessels, in which they tend to cause contraction instead of dilatation. The action of barium, however, on the muscular substance of the heart and vessels is alike, for in both it tends to cause prolonged contraction.[4]

One of the most powerful vaso-constrictants is adrenalin. It has the power of contracting all the vessels in the body with the exception of the intrapulmonary portion of the pulmonary artery, the coronary, and the cerebral arteries. In the two last it causes dilatation.[5]

Cocaine possesses the power of contracting the vessels in addition to its local anæsthetic action. A combination of adrenalin with cocaine forms a very powerful local anæsthetic, as the constricting action of the two drugs greatly lessens the local circulation, and thus prevents cocaine from being carried away and allows it to exercise prolonged anæsthetic action.

Pituitary extract has an action somewhat similar to that of adrenalin, but it is not so powerful nor so prolonged, and less certain, sometimes causing dilatation instead of contraction.[6] All substances belonging to the digitalis group have a certain power of contracting the vessels locally. With small doses the contraction is limited to the intestinal vessels, while

the renal vessels become dilated; with larger doses the renal vessels also become contracted.[7]

Central.—All drugs which in large quantities have a convulsant action, such as strychnine and pikrotoxin, stimulate the vaso-motor centre, and those tend to cause contraction of the blood-vessels and raise the blood-pressure. All the vessels of the body are not equally affected by strychnine. Those of the splanchnic area are affected more than the others, but, unlike digitalis, which tends to dilate the vessels of the kidney, strychnine causes them to contract.[8]

Caffeine has an action upon the vaso-motor centre similar to that of strychnine, but it acts locally on the periphery vessels in exactly a contrary manner, tending to dilate them. Camphor also stimulates the vaso-motor centre and renders it more sensitive to reflex stimuli, while the vessels of the splanchnic area are contracted by it. The vessels of the skin are dilated.

Alcohol produces dilatation of the peripheral vessels, and tends to lower the blood-pressure, while at the same time it stimulates the heart.[9]

Vaso-dilators. History of their Discovery.—The first vaso-dilator investigated was nitrite of amyl. Its power of causing flushing of the face was noticed by Guthrie in 1859,[10] and Dr B. W. Richardson observed that it caused dilatation of the capillaries in the frog's foot; but it was Dr Arthur Gamgee who first discovered its power of lowering the blood-pressure. It was under his direction that I had been carrying out my experiments on digitalis in the late Professor Douglas Maclagan's laboratory, and

I used to submit myself to Dr Gamgee for experiments upon the effect of nitrite of amyl on my own pulse, from which he made sphygmographic tracings. These experiments naturally rendered me thoroughly conversant with its physiological action on the pulse. The numerous observations I had made upon my own pulse naturally made me rather expert in the use of the sphygmograph; and when resident in the Royal Infirmary at Edinburgh I made a number of observations upon a case of angina pectoris which was at that time in the wards. I found that during every attack the tension of the pulse became greatly increased, and as the pain passed off the tension fell. Every remedy had been tried in vain, and the patient was just going out of the hospital when it occurred to me that if one could lower the pressure in his vessels one would very probably relieve his pain. I therefore kept him in one day longer to try the experiment, and promised him that if it should fail he should go out next day. To my delight the experiment proved a complete success. As I administered the nitrite of amyl, which my friend Dr Gamgee had given me, the patient's face became flushed, the pulse, instead of being small and thready, became full and bounding, and the pain almost instantaneously disappeared.[11] Nitrite of amyl still holds its place in medical practice as the most rapid and powerful vascular dilator, but other nitrites or nitrates having a slower but more lasting action have now come into more general use. In 1876, along with Mr Tait,[12] I discovered that nitroglycerine had an

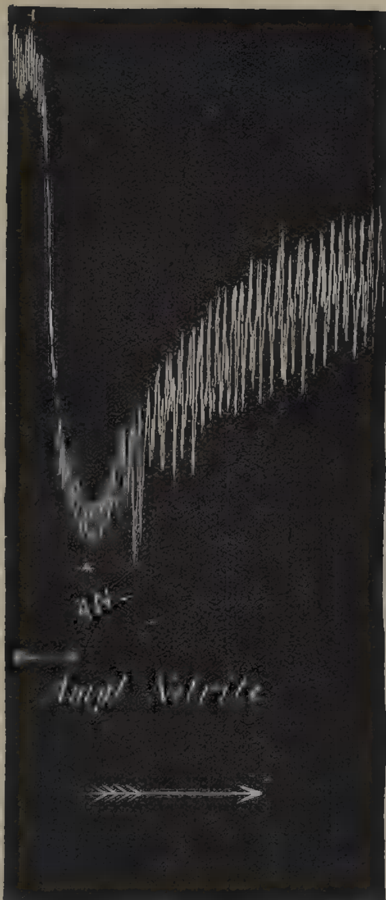


FIG. 100.—Tracing showing the action of amyl nitrite on the blood-pressure. The point where the administration was begun is marked by a cross; the point where it was discontinued, by a small arrow. The horizontal double-headed arrow indicates the zero point of pressure; the single-headed arrow indicates the direction in which the tracing is to be read.

action upon the circulation similar to that of nitrite of amyl, but I used to get such an awful headache from working with it that I hesitated to give it to patients, and while I was still hesitating Dr Murrell employed it in a case of angina with great success.[13] It has now become the stock remedy for lowering arterial tension, and has been introduced into the *British Pharmacopœia* in the form of tablets containing a hundredth of a grain in chocolate. These may be either taken at once, or a little bit of them may be nibbled, and the nibbling carried on until the pain passes off. If one is not sufficient, more may be used. Whilst working in Professor Ludwig's laboratory in 1869, I found that sodium nitrite had a similar action to amyl nitrite, but not so marked. This observation was not published, and the action of sodium nitrite was described some years later by Prof. M. Hay.[14] In 1876 and 1877 I made also a large number of experiments, along with the late Dr Gresswell of Melbourne, on the action of other nitrites, but owing to various circumstances these results also have not been published. A very interesting research by Professors Cash and Dunstan[15] on various nitrites shows that they are all alike in the nature of their action, though differing somewhat in degree. The same is the case with a substance differing entirely from them chemically, namely, hydroxylamine, which Mr T. J. Bokenham and I found to dilate the vessels, and produce a fall in the blood-pressure almost identical with that caused by nitrate of amyl.[16]

A most interesting discussion of the drugs

belonging to the nitrous group is contained in the lectures of the late Professor Leech,[17] whose death was a loss to the whole scientific world, and a great personal grief to everyone who knew him. Nitroerythrol is another substance which is almost more useful than any of the other nitrites, because its action, though less powerful, is more prolonged than theirs, and in cases where we wish to keep the blood-pressure constantly low it is very convenient, an eighth to half a grain or even more being taken every two, four, or six hours, more or less, as the case requires. Nitromannitol may also be used in doses of one grain or more. Where the pulse is very quick, aconite or colchicum may be given and general bleeding may be required.

Classes of Vaso-dilators.—The chief vaso-dilators are amyl nitrite and other nitrites belonging to the aliphatic series and nitrites of the alkali metals, the chief of those being nitrite of soda. Some nitrates, such as nitroglycerine, nitroerythrite, nitromannitol, although they are nitrates, have a rapid effect on the blood-pressure, and so has hydroxylamine. Nitrates such as nitrate of potash seems to have an action of the same sort, though not so rapid or powerful, but is longer continued. In full doses they all act directly upon the capillaries, causing them to dilate; but in the case of nitrite of amyl, and probably the other aliphatic nitrites, the dilating centre in the medulla appears to be affected first, so that the dilatation is of two-fold origin, central and peripheral. Another group of vaso-dilators contains benzoates and hippurates.

The kidney possesses a remarkable reciprocating action in regard to the benzoates, for Schmiedeberg has found that if benzoic acid is added to the blood perfused through the kidney, hippuric compound appears in the urine, while if hippuric acid is added to the blood, benzoic acid appears in the urine.[18] Guipsine is obtained from mistletoe, and is said to have a dilating effect upon the vessels, so that it reduces blood-pressure.[19]

Iodides.—Iodides differ from vaso-dilators already mentioned in so far that when injected into a vein they have no immediate effect on the blood-pressure,[20] but when administered for a length of time they certainly appear to lower it. The most commonly used is the iodide of potassium, but if the heart be feeble and the depressing effect upon the heart at all feared, the iodide of sodium may be used in its place. One drawback to the use of either iodide of potassium or sodium is its exceedingly disagreeable taste, which remains almost constantly in the mouth. The reason of this is that the iodides are secreted with extreme rapidity by the salivary glands. The saliva is swallowed, absorbed by the stomach, and again excreted by the saliva, so that its taste remains in the mouth a long time. Iodides have also the power of causing other substances which are not usually secreted by the salivary glands to pass into the saliva. Thus Claude Bernard [21] found that when lactate of iron was injected into the artery of the submaxillary gland, it did not appear in the saliva, but did so if it was mixed with a solution

of iodide of potassium previous to injection. I think that iodides exercise a similar effect upon quinine, because the out-patients at St Bartholomew's Hospital almost unanimously refused to take a draught containing quinine with iodide of potassium, on account of the bitter taste being present in the mouth the whole day. Some patients complain of a similar bitter taste during the use of iodides although these are not accompanied by any bitter medicines. In such cases I am inclined to think that the bitter taste is due to some autotoxin—perhaps peptotoxin—or other bitter substance in the bile, and a mercurial purgative followed by a saline may remove it. The taste may be covered to a considerable extent by means of saccharin, the quantity required being in proportion to the dose of iodide. Chloroform water also covers the taste, and so does liquorice. Some patients dislike the taste and look of liquorice, so that iodide of potassium given with chloroform water and a little tincture of lemon or orange to cover the taste makes an elegant prescription. After a good many trials I find the following prescription to be the best :—

℞ Potassii iodidi	.	gr. v.
Tinct. Limonis	.	ʒss.
Elixir glusidi	.	♏v.
Aquam .	.	ad ʒj.

Ft. Mist. M.

Each fluid drachm contains 5 grs. of potassium iodide According to the dose desired, 1, 2, 3, or 4 fluid drachms are to be taken in half a tumblerful or more of soda water. It is most convenient to have the soda water in a syphon, and having put the requisite

quantity of the iodide solution in a tumbler, to add the soda water and drink during effervescence. Some patients find that 5 minims of elixir glusidi make the mixture too sweet, and for them the quantity may be lessened whilst a larger quantity of lemon, such as 1 fluid drachm of the tincture, is more pleasing to the palate. Iodide of sodium may be used in place of iodide of potassium when desired. As the medicine has frequently to be taken by patients suffering from arterio-sclerosis three or four times a day for many weeks at a time, it is of considerable importance that the form in which it is administered shall be as little disagreeable as possible.

Iodide is generally given in doses of 5 to 10 grs. three times a day, but in some cases it answers as well, or better, to give a dose of 30 grs. at bedtime. In some people it brings on running at the nose and salivation, and in one case I have seen it produce abdominal pain and tenderness all over the pancreas and limited to it, as if its action on the pancreas had been the same as on the salivary glands. The curious point is that while 2 or 3 grs. cause the nose to run very freely, 20 grs. rarely do so, so that the coryza may be stopped either by giving up the medicine or by doubling the dose. With very large doses pustular eruptions are likely to occur, and to prevent these small doses of arsenic are frequently given along with the iodide. Locally the pustules may be treated with an antiseptic ointment, such as carbolic acid ointment, and ointment of ammoniated mercury may also be employed, but should only be tried on a few at a time, as it may possibly give rise to increased irritation.

The Effect of Drugs upon the Coronary

Arteries.—If the coronary arteries were affected by drugs in the same way as the other vessels, the consequence would be that just at the time when the blood-pressure was raised throughout the body the supply of blood to the heart would be diminished, and the power of the heart consequently lessened at the very time it was called upon to do more work. But the contrary is the case, and many drugs which contract the vessels of the rest of the body cause dilatation of the coronary arteries. The way in which the action of drugs upon these vessels is usually investigated is to put a cannula into one of the branches of the coronary artery and note the rate at which blood flows out before and after the administration of the drug. The experiments are made either upon the heart *in situ* or removed from the body and perfused with a nutrient fluid. When the experiments are made upon the heart *in situ*, the result is a mixed one, for it depends not only upon the size of the coronary vessels, but upon the general blood-pressure which drives the blood through this. Thus a drug which raises the general blood-pressure, such as digitalis, may increase the rapidity of flow through the coronary arteries without really dilating them, because while their size remains the same, the greater pressure of blood in the aorta will naturally drive more blood through them in a given time. In the same way a drug, such as nitrite of amyl, may lessen the amount of blood passing through the coronary arteries even though it actually dilates them, because it lowers the blood-pressure in

the aorta. In experiments upon an excised heart this factor can be eliminated, because the pressure under which the perfused fluid is forced through the heart may be kept alike. The coronary artery is dilated by adrenalin, by the digitalis group of substances, by caffeine, and by theobromine.[22] It has been said by G. S. Bond that the out-flow from the coronary veins is lessened by nitro-glycerine and amyl nitrite.[23] As I have already explained, however, this lessening may be due to a simple fall of the general blood-pressure; and in one experiment made by Professor Kronecker and myself, we found that the out-flow was increased enormously by amyl nitrite, notwithstanding the general fall of blood-pressure. Such a dilating action of amyl nitrite and nitro-glycerine upon the coronary vessels would readily explain the relief they offer in angina pectoris, even in cases where the blood-pressure is normal.

LITERATURE.

1 D. Cow, *Journ. of Physiol.*, 1911, vol. xlii., p. 132.
2 Ludwig and Mosso, *vide* Lauder Brunton, *Text Book of Pharmacology, Therapeutics, and Materia Medica*, 1885 (Macmillan & Co.), p. 241.
3 Gaskell, *Journ. of Physiol.*, 1880-2, vol. iii., p. 53.
4 Boehm, *Arch. f. exper. Path. u. Pharm.*, 1875, Bd. iii., p. 216; Ringer and Sainsbury, *Brit. Med. Journ.*, 1883, vol. ii., p. 265; D. Cow, *loc. cit.*, p. 134.
5 D. Cow, *loc. cit.*, p. 132.
6 D. Cow, *loc. cit.*, p. 134.
7 Gottlieb and Magnus, *Arch. f. exper. Path. u. Pharm.*,

1901, Bd. xlvii., p. 135; Loewi and Jonescu, *ibid.*, 1908, Bd. lix., p. 71.
[8] Wertheimer und Delezenne, *Compt. rend. d. l. Soc. de Biol.*, 1897, p. 633.
[9] Meyer and Gottlieb, *Exper. Pharmakologie*, 1910, pp. 232-3.
[10] F. Guthrie, *Journ. of Chem. Soc.*, 1859, vol. xi., p. 245.
[11] Lauder Brunton, *Lancet*, 27th July 1867, p. 97; reprinted in *Collected Papers*, First Series, p. 137 *et seq.*
[12] Brunton and Tait, *St Bartholomew's Hospital Reports*, 1876, vol. xii., p. 144; reprinted in *Collected Papers*, First Series, p. 474 *et seq.*
[13] W. Murrell, *Lancet*, 1879, vol. i., pp. 80, 113, 151, 225.
[14] M. Hay, *Practitioner*, vol. xxx., pp. 179-194, 321-330; *Brit. Med. Journ.*, 1883, vol. ii., p. 1095.
[15] Cash and Dunstan, *Phil. Trans.*, 1893, vol. clxxxiv., pp. 505-639.
[16] Brunton and Bokenham, *Roy. Soc. Proc.*, 1889, vol. xlv., p. 352.
[17] D. J. Leech, *Pharmacological Action and Therapeutical Uses of the Nitrites and Allied Compounds.* Edited by R. B. Wild (Manchester: Sherratt & Hughes, 1902).
[18] Bunge and Schmiedeberg, *Arch. f. exper. Path. u. Pharm.*, 1877, Bd. vi., p. 233; Schmiedeberg, *ibid.*, 1881, Bd. xiv., pp. 288, 379.
[10] Gaultier and Chavalier, *Compt. rend.*, 25th Nov. 1907, vol. cxlv., p. 941; O. K. Williamson, *Practitioner*, 1911, p. 690.
[20] Stockmann and Charteris, *Brit. Med. Journ.*, 1901, vol. ii., p. 1520.
[21] Claude Bernard, *Leçons de Physiol. expérimentale*, 1856 (Paris: J. B. Baillière), Tome ii., p. 99.
[22] D. Cow, *loc. cit.*, p. 132 *et seq.*
[23] G. S. Bond, *Journ. of exper. Medicine*, 1910, vol. xii., pp. 580-1.

CHAPTER XV

ACTION OF DRUGS ON URINARY, DIGESTIVE, AND NERVOUS SYSTEMS

Drugs acting on the Kidneys, Digestive Organs, and Nervous System—Diuretics—Mercury as a Diuretic—Uses of Tapping—Purgatives—Mercurials—Gastric Disinfectants — Swallowing Air — Alkalies — Sour Milk — Intestinal Disinfectants — Carminatives — Adjuvants to Carminatives—Narcotics.

Diuretics.—The secretion of urine depends to a great extent on the pressure of blood in the glomeruli of the kidney, and Ludwig[1] showed that, as a general rule, the higher the pressure within the glomeruli, the more rapid is the secretion of urine. This is generally known as Ludwig's theory of the secretion of urine. For a number of years he looked upon the transudation of fluid through the glomeruli under pressure as the main factor in secretion, and thought that the fluid thus exuded underwent concentration by absorption of its watery constituents in its passage through the tubules. In 1870, however, he modified his theory considerably in the direction of Bowman's original one,[2] so that latterly Bowman and Ludwig's theories very nearly coincided. Bowman held

that the watery part of the urine transuded from the glomeruli, while the solid constituents were excreted by epithelium of the tubules. Bowman came to this conclusion on anatomical grounds alone, while Ludwig founded his theory on actual experiment. The proportion of salts and of water which the kidney must excrete in order to maintain the proper proportion of these in the body varies enormously under different conditions. Thus people living on a more or less liquid diet, with a small proportion of proteins, such as a diet consisting of bread, butter, tea, and farinaceous foods generally, with a little milk, must excrete a large quantity of water and only a very small proportion of urea, or other products of nitrogenous waste. On the other hand, especially if the skin is acting but slightly, people living in hot climates, such as South Africa or South America, living upon a highly nitrogenous diet, such as dried meat, and with a small proportion of water, must retain water as much as possible in their bodies, and at the same time excrete a large quantity of urea. In the kidney we find a provision by which this can be effected. Not only can the vessels of the kidney be dilated by the action of drugs while other vessels throughout the body are contracted, but the kidney contains some mechanism by which the blood going to it through the renal artery may be sent at one time almost exclusively through the glomeruli, so that much water can be excreted and little solid; and at another time almost exclusively to the

tubules, so that much solid can be excreted and but little water. This can be more easily understood by the help of a diagram of Hans Meyer's.[3]

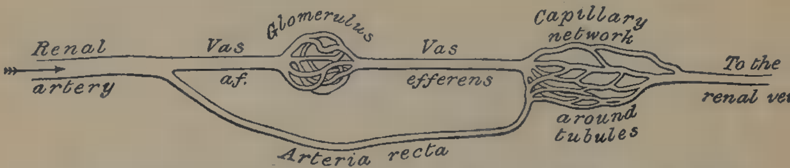


FIG. 101.—Diagram to show the by-pass whereby blood may go to the plexus surrounding the tubules and supply material for excretion of solids without passing through the glomerulus and losing water. (After Meyer and Gottlieb.)

We may divide diuretics into five groups:—

1. What we may call the natural diuretics,

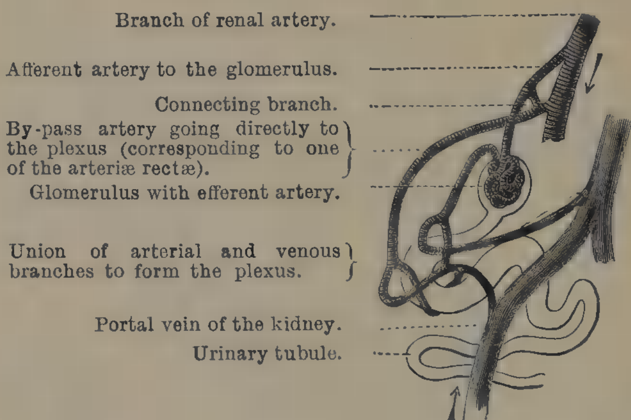


FIG. 102.—Diagram of the circulation in the kidney of the newt. Modified from Nussbaum, and arranged to show the parts of the kidney which are probably affected by different diuretics. (From Lauder Brunton's *Pharmacology and Therapeutics*, p. 378, 1st Ed. London: Macmillan, 1885.)

water, urea, and purin bodies allied to it (p. 317), caffeine, theobromine, theophylline,

and theocin. These bodies increase the rapidity of the circulation through the kidney, and increase the amount of water poured out through the glomeruli, but at the same time they probably interfere with the reabsorption in the tubuli, as indigo carmine injected along with caffeine does not appear in the epithelium of the tubules as it would do if injected alone. In all probability, however, caffeine not only tends to prevent reabsorption, but to stimulate secretion by the cells of the tubules.

2. The second and third groups alter the circulation in the kidney. The second group contains the substances which, like digitalis, dilate the vessels of the kidney but also at the same time contract those of the body generally. The blood is thus driven under a higher pressure than normal through the dilated afferent arteries of the kidney, so that the circulation through the organ becomes much more rapid, and the secretion of urine very greatly increased. The dilating effect upon the renal arteries may be sufficient to produce diuresis, although the contraction of arteries in the rest of the body may not be sufficient to raise the blood-pressure. When the drugs are given in too large doses, they may cause such great contraction of the renal vessels as to arrest the circulation and stop the secretion of urine.

3. The third group contains those drugs which dilate the vessels of the body generally, including those of the kidneys. Such substances may dilate the vessels of the kidney so

much as to produce diuresis in spite of lowering the blood-pressure generally. Thus nitrite of ethyl in the form of nitrous ether has long been recognised as a most useful diuretic, and nitrite of soda increases the secretion of urine even when the blood-pressure is below normal.

4. The fourth group contains the ethereal oils, such as oil of juniper. I do not know that the mode of action of these has been precisely ascertained, but in all probability they act upon the tubules.

5. The fifth division of diuretics is that of salines, such as potassium tartrate, and acetate, and also sodium sulphate. According to Meyer and Gottlieb, these salines have an action on the kidney similar to what they have on the intestine, causing secretion in one part and preventing absorption in another. In the kidney they probably increase the exudation of fluid through the glomerulus and prevent its reabsorption in the tubule, or, as Meyer puts it, they cause diarrhœa of the tubules.[4]

Mercury as a Diuretic.—The effect of small doses of mercury and calomel in producing or increasing diuresis has long been known, and one of the best diuretics in cardiac disease is certainly the old-fashioned pill, which is 1 gr. each of powdered digitalis, squill, and blue pill. The action of calomel is said by Fleckseder[5] to be due to the profuse secretion of saliva and intestinal juice, which lessens the proportion of water in the blood, and thus leads to absorption from œdematous tissue. If the watery contents of the intestine are evacuated there is no

diuresis, but if they are retained, the kidneys excrete the extra amount of water, and thus calomel diarrhœa and calomel diuresis are vicarious. This hypothesis is not quite satisfactory because the beneficial effect of mercury in aiding diuresis frequently, indeed generally, occurs without any apparent increase of the salivary secretion. Locke's idea is that mercury acts indirectly on the urine by increasing the formation of urea in the liver, and the larger amount of urea acting as a diuretic.[6]

It is just possible that the effect of mercury may be due to some alteration which it produces in the vicosity of the blood and consequent freedom of flow through the glomeruli of the kidneys. The exact action of mercury on the blood is not at present known, but it is evident that when pushed to the extent of salivation it was found to have a profound effect upon the blood, as shown by the alteration it produced in its characters at the time when blood-letting was frequently used along with salivation.

Uses of Tapping.—The secretion of the kidney depends very greatly upon the rapidity of the circulation through it, and if either the veins or the tubules are obstructed, pressure is exerted on the glomeruli, and the circulation is greatly diminished with consequent lessening in the amount of urine secreted. The backward pressure of the blood in mitral disease tends to increase the pressure in the veins, as shown in B, Fig. 103, and this not only compresses the arterioles but leads to albuminuria. A similar

effect is produced by obstruction to the flow of urine through the ureter, and consequently through the tubules, as shown in C, Fig. 103. When the abdomen is distended with ascites, pressure is exerted both on the renal veins and

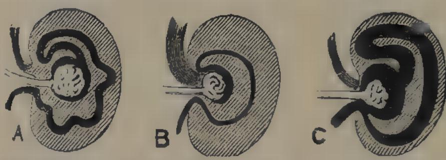


FIG. 103.—Diagram to show the effect of venous congestion and of obstruction of the ureter or tubules on the kidney. A, normal kidney, with artery in the centre of the hilus. The artery ends in a glomerulus from which a urinary tubule passes into the ureter, which is shown passing out of the hilus below the artery. The renal vein is shown above the artery in the hilus. B shows congestion of the vein, with consequent compression of the artery and tubule. C shows obstruction of the ureter and tubules.

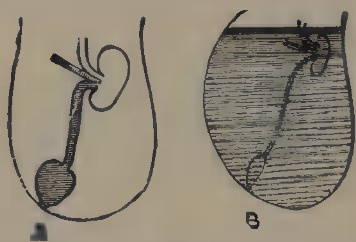


FIG. 104.—Diagrammatic section of the abdomen: A, in the normal state; B, in advanced dropsy, where the ascitic fluid compresses the kidney itself and also the ureter, so that the secretion of urine is hindered in two ways: (1) by pressure on the outside of the kidney, and (2) by pressure on the inside of the kidney from the tension in the urinary tubules.

on the ureter (Fig. 104), and thus diuretics may fail to act unless the pressure is removed by tapping.

Purgatives. — Free purgation not only removes the intestinal contents quickly and

prevents to a considerable extent the formation of toxamines, but some purgatives cause great secretion of watery fluid in the intestine, and thus lessen the proportion of water in the blood. In consequence of this, absorption takes place from the œdematous tissues. The best of such hydrocathartics which has retained its place in practice for many years is the compound jalap powder. The bitartrate of potash which it contains tends to produce a flow of watery fluid into the intestine, while the jalap by stimulating intestinal peristalsis causes the water to be evacuated and prevents reabsorption. The action of the jalap powder may be increased by giving a teaspoonful of potassium bitartrate along with the usual 30 grs. of the compound jalap powder. Elaterium or compound powder of elaterin is a very powerful hydrocathartic, but on account of the depression it produces must be used with more care, and is not so well adapted for general use as the compound jalap powder. There is a considerable difference between the action of such purgatives as those just named and mercurials. These act generally upon the lower parts of the small and the whole of the large intestine. They have not the same action as mercurials upon the removal of bile.

Mercurials.—They do not really increase the secretion of bile; on the contrary, they may lessen it, but they do appear to have the power of removing bile from the body. It has been shown that the green motions which so often occur after calomel owe their colour to bile. By removing bile from the body one is able to

remove also the toxins which may be contained in the bile. Various toxins formed in the intestine as well as poisons which have been ingested are absorbed from the intestine and carried by the portal vein to the liver and are excreted in the bile, in which they pass again

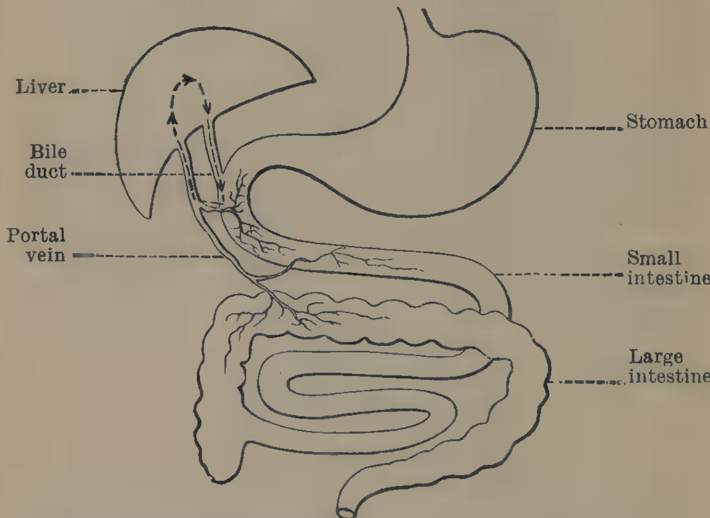


Fig. 105.—Diagram to illustrate the entero-hepatic circulation and retention of bile and toxins in the body.

to the intestine. There they undergo absorption a second time, and in this way poisons may circulate for a long time from the intestine to the liver and back again without leaving the body, although small quantities may be constantly passing into the blood. Probably it is by the removal of toxins that mercury in its various preparations proves such a useful adjunct to other drugs in the treatment of

disorders of the circulation. Its action should be supplemented by some saline to sweep the toxins out of the intestines, as if they remain in the upper part they may again undergo reabsorption.

Gastric Disinfectants.—Most toxins belong to the aromatic series and are derived from albuminoid bodies. The chief gases in the intestine are carbonic acid and marsh gas, and these are formed chiefly by the fermentation of carbohydrates. Normal gastric juice has an antiseptic action, and when the food is well digested in the stomach there is less chance of either toxins or gases being formed from it in the intestine. If the gastric juice, however, is much diluted by fluid taken during the meal it will not exert this action, and in addition the albuminous food will be less broken up in the stomach and pass into the intestine in larger masses. One great rule to prevent flatulence, therefore, is to give solids and liquids separately, and if this is not sufficient to prevent fermentation it may be advisable to give carbohydrates such as bread and starchy food at one meal, and proteins such as eggs, milk and cheese at another. In all cases it is advisable to have the food thoroughly masticated before it is swallowed. It is to be remembered that when gastric digestion is active the production of gas either in the stomach or intestine is likely to be diminished, and the administration of pepsin or other digestive ferments tends both to help the digestion of the food and lessen the production of gas.

Swallowing Air.—This is another cause of flatulence. It occurs frequently from irritation of the stomach by acidity, so that more saliva flows into the mouth, and this occasions a constant tendency to swallow. Flatulence arising from this cause is often prevented by the use of bismuth and bicarbonate of soda to lessen the irritation in the stomach. The most common gastric antiseptics are sulpho-carbolate of soda in doses of 5 to 15 grs., carbolic acid in doses of 1 to 3 grs. in the form of pill or capsule, creasote 1 to 5 minims usually given in capsule, naphthol in doses of 3 to 10 grs. in a cachet. Beta-naphthol is more commonly employed than alpha-naphthol, for though the latter is a stronger and more powerful antiseptic, it is more irritating to the stomach. Vegetable charcoal is a useful remedy, and may be given in the form of biscuits or powder. The powder may be simply mixed with water or swallowed in a cachet or, what is easier, given as a wafer. Peroxide of magnesia is both antiseptic and antacid. It is usually given in doses of one-third of a teaspoonful with water or it may be combined with charcoal. Some biscuits are in the market containing these two substances.

Alkalies.—When much acid is present in the stomach, it may cause a good deal of reflex irritation, and possibly may even lead to cardiac disturbance and faintness (p. 179). It is most readily neutralised by means of bicarbonate of soda, of which half a teaspoonful or even more may be put into a tumbler of water, and slowly sipped till the desired result is obtained. The

disagreeable taste of this is to a great extent removed, if a small crystal of citric acid is dropped into the tumbler. This causes the disengagement of carbonic acid, and this effervescent mixture is much pleasanter than the simple solution. The carbonic acid also tends to make the bicarbonate dissolve more readily, and quite a small crystal of citric acid is sufficient, so small as by no means to neutralise a quarter of the bicarbonate. This mixture frequently acts as a powerful carminative, and if desired may be given along with other carminatives. Half a teaspoonful or a teaspoonful of sal volatile in 2 or 3 ozs. of water may also be used in place of the bicarbonate of soda, and has a more stimulating action on the heart if this should be feeble. Magnesium hydroxide also acts as a powerful antacid, and may be given in almost any quantity, though usually half a teaspoonful to two teaspoonfuls is sufficient. In the form of magnesia cream it is more palatable than in the form of the dried powder. The effect of alkalies, which at the same time act as carminatives, upon irregular action of the heart or tachycardia is sometimes extraordinary, the intermittence disappearing, or the pulse returning to its normal rate almost immediately after the expulsion of a large volume of flatus from the stomach, and the consequent removal of reflex irritation of the heart through the gastric branches of the vagus (Fig. 106).

Sour Milk.—The gases which produce flatulence in the intestine are chiefly marsh gas and carbonic acid. The substances from which they

are most readily produced are the carbohydrates, such as starch, sugar, and cellulose. Milk sugar is not so readily fermented as other sugars, and milk in its ordinary state when taken without any carbohydrates does not, as a rule, produce flatulence, and a few days of pure milk diet may greatly lessen the production of gas. According

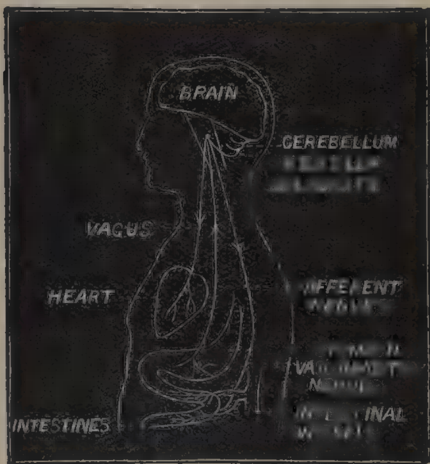


FIG. 106.—Diagram to show the nervous mechanism by which the action of the heart may be depressed by irritation of the stomach. The reflex irritation of the vagus may render the heart's action simply weak, or slow and weak.

to Metchnikoff[7] the lactic acid bacillus tends to destroy other bacilli of a pathogenic nature in the intestine, and thus to prevent the formation of toxic products. Milk which has been rendered sour by the addition of the lactic acid bacillus thus tends to sterilise, in a measure, the whole intestinal tract by destroying all other bacilli excepting .itself. It is best to render the milk

acid by the addition of the bacillus acidi lactici before giving it, but sometimes when this can not be done the lactic acid bacillus may be given in tablets; but this method of giving it is not so satisfactory. It is very important that a pure strain of the bacillus should be obtained, because if the bacillus butyricus is mixed with it, it renders the milk not only offensive to the taste and smell, but very irritating to the stomach and intestines. Milk may be readily soured each time by the addition of bacilli in tablets to the fresh milk; but instead of this it is better when once a good strain of sour milk has been obtained, to add a little of it to the fresh milk instead of adding new tablets.[8]

Intestinal Disinfectants.—The same disinfectants which are useful for the stomach are also useful in the intestine. One of the most powerful perhaps is mercury in various forms. A solution of the perchloride is sometimes useful, in doses of half a drachm to a drachm repeated every four to six hours. It has a very disagreeable taste, so it is preferable to give it in the form of pill in the dose of one thirty-second to one-sixteenth of a grain instead of in solution. Calomel or grey powder sometimes acts quite well from the conversion of minute portions into perchloride. One-tenth of a grain of calomel every hour or the third of a grain of grey powder is sometimes very useful, especially if the liver be somewhat full and tender. Naphthol is useful for the intestine as well as for the stomach. Salol is a useful intestinal disinfectant in doses of 5 or 10 grs. in cachet

about every six hours. It is not decomposed by acids but is decomposed into phenol and salicylic acid by alkalies, and, therefore, should not be given along with them. If the motions are very offensive the odour is removed perhaps more quickly by naphthalin than by any other drug. It has, however, such an exceedingly disagreeable and penetrating odour that almost the only way to give it is to have it put up in powders, and when these are administered a large wafer should be ordered and the powder should be shaken upon it, the wafer wrapped up and swallowed at once. When it is put up in cachet the odour penetrates through the cachet.

Carminatives.—These are medicines which tend to cause evacuation of flatulence either from the stomach or bowels. The most commonly used are essential oils, either given in small quantities in the form of a pill or more frequently dissolved in alcohol or water in the form of spirits or waters. The oils used for this purpose are oleum anethi, anisi, anthemidis, cajuputi, carui, caryophylli, cinnamomi, coriandri, lavandulæ, menthæ piperitæ, menthæ viridis, myristicæ, pimentæ, rosmarini, terebinthinæ. The spirits are spiritus ammoniæ aromaticus, ammoniæ fœtidus, ætheris, ætheris co., anisi, cajuputi, camphoræ, chloroformi, cinnamomi, juniperi, juniperi co., lavandulæ, menthæ piperitæ, menthæ viridis, myristicæ, rosmarini. The waters are aqua anethi, anisi, camphoræ, carui, chloroformi, cinnamomi, fœniculi, menthæ piperitæ, menthæ viridis, pimentæ. In addition to these may be mentioned the

compound tincture of cardamoms and the tincture of ginger. Asafœtida is one of the most powerful carminatives but its smell is exceedingly disagreeable. In the form of the compound galbanum pill it is sometimes very useful in intestinal flatulence. When there is much intestinal distension the most useful remedy one can employ is asafœtida in the form of an enema. This used formerly to be made by rubbing up 30 grs. of asafœtida with 4 ozs. of distilled water, but is more easily made by adding a teaspoonful of tincture of asafœtida to 4 ozs. of thin starch paste.

Dill water in the form of an enema sometimes brings away flatulence rapidly from the intestine. It may be given either alone in doses of 4 ozs. or more, or made up to 8 or even 16 ozs. with thin starch paste and injected at once. The most common of all carminatives is probably peppermint water, and the action of this is frequently assisted considerably by adding to half a wine glassful 10 or 15 grs. of bicarbonate of soda or about half a teaspoonful of aromatic spirits of ammonia. Such a dose may be repeated if necessary every quarter of an hour until relief is obtained. Another favourite remedy is the syrup or tincture of ginger in doses of half a teaspoonful to one teaspoonful in about a wineglassful of water or five to ten drops of the strong tincture, or essence as it is usually called, given in the same way. Five or ten drops of oil of cajuput given in the same way or simply dropped on a piece of sugar and sucked is occasionally very useful.

Another pleasant remedy is half a drachm or a drachm of compound tincture of cardamoms in an ounce of chloroform water, and the addition of 10 minims of the spirit of ether assists its action. Dill water is used almost universally as a carminative for infants, and is, I think, too much neglected as a carminative for adults. It may either be given alone or with some of the carminative spirits and tinctures already mentioned.

Adjuvants to Carminatives. — Sometimes flatulence may be relieved by passing a long india-rubber tube well up the rectum, and, if possible, into the sigmoid flexure. For this purpose I think a long stomach-tube is better than rectal tubes, or even catheters, because the rectal tubes usually have a sharp end which does not find its way so well up the bowel as the blunt end of the stomach-tube. A large tube is frequently more easy to pass than a small one, as the small ones double up and become kinked in the rectum. The accumulation of gas in the intestine is frequently due, in part, at least, to weakened expulsive power of the muscular wall of the intestine. It has been found that such paresis of the intestine, a condition which very commonly comes on and gives rise to abdominal operations, can be relieved or removed by the use of pituitary body, and this can be given either by the mouth or perhaps better by the injection of $7\frac{1}{2}$ to 15 minims of a 20 per cent. extract. This is best injected into the muscles, as when injected hypodermically it may cause sloughing of the skin and vaso-motor constriction.

Narcotics. — One of the most distressing symptoms in various diseases of the heart and vessels is sleeplessness. Sleep appears to depend upon a quiescent condition of the cerebral vessels, and may be brought about by the action of such drugs as lessen their functional activity even though the cerebral circulation be unchanged. According to Bouchard,[9] the normal alternation of sleep and waking is due to the formation in the body of certain substances which could hardly be called toxins but may be termed leucomaines. Those formed during the day have a soporific action, so that at night their accumulation tends to produce sleep. During night these narcotic substances are eliminated and stimulating substances are formed, so that by-and-by the narcotic action passes off and the stimulant action prevails, so that the person awakes. Amongst the narcotic products formed in the day is possibly lactic acid or lactates, which are the products of muscular waste. But these are certainly not the only ones. The condition of the nerve cells depends very much upon the circulation. Thus it was shown by Friedländer[10] that when the rabbit has received a dose of isopropyl alcohol it falls asleep at once when its head is held up and the circulation is lessened, but awakes at once when its head is lowered, so that the circulation in the brain is increased. In man, Durham[11] observed that the brain became anæmic during sleep and vascular on awaking. The circulation of blood in the brain is probably regulated by the contractile power of the carotids and their branches.

If the carotids are sclerosed so as to lose their contractile power, sleeplessness may occur as a consequence, and in one case of persistent insomnia I have seen sleep become restored when the vessels became less rigid from the combined action of local massage and the use of potassium iodide. Where the tension is very high the blood tends to pour through the carotids even in spite of their contraction, and thus people suffering from high tension are liable to be sleepless. A similar condition occurs in people with deficient vaso-motor power in whom the blood-pressure may be low, but the carotids are deficient in contractile power, and thus sleeplessness may be associated with high tension or with low tension. When the heart's action is excited by high temperature, as in fever or by the effect of drugs such as caffeine, the circulation through the brain is increased and insomnia results. Sixty years ago almost the only soporific known was opium, and in administering this physicians recognised the importance of circulation, because if the circulation was quiet opium was given alone, but if fever were present at the same time it was usually combined with tartar emetic. In one preparation, Dover's powder, which was greatly in vogue, the tartar emetic was replaced by ipecacuanha, and this still remains an exceedingly good remedy, because one of the dangers that is usually apprehended from opium is its depressing action on the respiratory centre, and this is counteracted to a great extent at least by the ipecacuanha, which has a stimulant effect upon this

centre. In cases where the kidneys are seriously diseased so that there is little power of excretion, small doses of opium sometimes produce unexpectedly powerful results, and a dose which would ordinarily be perfectly safe would be followed by fatal consequences. The cases in which this occurs are those in which the excretory power is lessened, but the mere occurrence of albumen in the urine in a case of mitral disease is not to be regarded as a contra-indication for opium.

LITERATURE.

[1] Ludwig, *Wagner's Handwörterbuch der Physiologie*, 1884, Bd. ii., p. 628 *et seq.*
[2] Bowman, *Phil. Trans.*, 1842, vol. cxxxii., p. 57.
[3] Meyer and Gottlieb, *Exper. Pharmakologie*, 1910, p. 297.
[4] *Ibid.*, p. 298.
[5] Fleckseder, unpublished research; *vide* Meyer and Gottlieb, *loc. cit.*, p. 299.
[6] Locke, *Practitioner*, 1886, vol. xxxvii., p. 170.
[7] Metchnikoff, *The Prolongation of Life*, trans. by P. Chalmers Mitchell (London: Heinemann, 1907).
[8] For literature, *vide* Martindale and Westcott, *Extra Pharmacopœia*, 15th ed., 1912, vol. i., p. 45 *et seq.*
[9] Bouchard, *Comptes rend.*, 1886, vol. cii., pp. 669, 727, 1127.
[10] Friedländer, *Über den Isopropyl Alcohol, Dissert.*, Berlin, 1888.
[11] Durham, *Guy's Hospital Reports*, 1860, vol. vi., p. 149; *Psychological Journal*, vol. v., p. 74 *et seq.*; *Brit. and For. Med. Chir. Rev.*, 1861, vol. xxvii., pp. 234 and 332.

CHAPTER XVI

TREATMENT OF ACUTE HEART DISEASE

Treatment of Acute Heart Disease—General Rules—Acute Rheumatism — Microbic Infection — Rest — Clothing—Sponging — Diet—Drinks—Stimulants—Flatulence — Medicines—Elimination—Local Applications—Poultices — Icebags—Leeches—Treatment of Convalescence.

IN the treatment of all cases of heart disease, whether acute or chronic, it has always to be borne in mind that there is a natural tendency to recover, and that this tendency should be assisted to the utmost by attending to

1. Rest,
2. Nutrition,
3. Elimination.

Rest to the heart is of the utmost importance, but it must not be forgotten that in the case of the heart, like that of a sprained ankle, too much rest may interfere with the nutrition. The nutrition of the heart depends partly upon its action, partly upon the condition of its vessels, and partly upon the nature of the blood with which it is supplied. In acute conditions there is a tendency to over-action of the heart, and therefore rest should be given to the

utmost extent; but in chronic conditions a certain amount of exercise is advisable, both as increasing the supply of blood to the heart in the manner already described (p. 155), and by its action on the other parts of the body increasing digestion, absorption, and elimination of waste. In many cases of heart disease attention to the digestion and elimination is of even more importance than the use of remedies which will act directly upon the heart.

Acute Cardiac Diseases.—A few patients die of acute myocarditis, endocarditis, or pericarditis, but the great majority of all cases of organic heart disease do not die when first attacked but after a more or less prolonged period, sometimes lasting for many years, from the consequences of valvular disease occurring during such an attack. Endocarditis, pericarditis, and myocarditis frequently occur in the course of rheumatic fever or acute infective diseases, and it is, therefore, most important to watch for the first approach of a cardiac affection and take measures to prevent injurious consequences. When the first sound of the heart becomes weak or imperceptible, or the pulse begins to get exceedingly feeble, rapid or irregular, suspicion is at once directed to the heart, and sometimes the thermometer may be most useful in detecting the mischief. When the temperature is taken, as is often done, only night and morning, a deceptive record may be obtained, because it may appear perfectly normal; but in endocarditis the temperature frequently shoots up some time during the day, and

if a four-hour record is taken this may be detected.[1]

Cardiac disease certainly seems to be greatly on the increase, but how far this is due to the increased power of detection, owing to increased medical training and to the improved use of diagnostic methods, and how far to actual increase in the number of cases it is hard to say.

It is quite possible, however, that the difference in the treatment of rheumatic disease fifty years ago and now may be responsible for the increased amount of cardiac mischief. Formerly a case of rheumatic fever was treated by alkalies, usually in the form of citrate of potash and by blisters over the affected joints, but the course of the disease was slow and the enforced rest in bed was necessarily long. Nowadays by treatment with large doses of salicin compounds, the pain in the joints quickly disappears, and the patient is often able to get about in a few days instead of weeks or months. It is by no means improbable that the strain which rising so soon produces upon the heart, enfeebled by the disease and perhaps also to some extent by the remedies employed, may be responsible for a good deal of cardiac mischief. Certainly cases of influenza seem to bear out this opinion very strongly, because I have frequently noticed that patients have complained of symptoms of feeble circulation which came on after influenza and have lasted two, three, or even more years, and these symptoms have come on not unfrequently after mild attacks of influenza in

which the patient was either not confined to bed at all or only for a short time. I think it quite likely that if the voluntary muscles were not also enfeebled by an attack of typhoid, this disease would be followed by cardiac symptoms more frequently than it is at present.

As Caton[2] has well pointed out, cardiac excitement while endocarditis is present is likely to hammer the pathogenic microbes into the valves and thus lead to valvular disease. It is, therefore, of the utmost importance that the patient should be kept at absolute rest. The rules for this have already been given (*vide* p. 232).

Rest.—Any excitement will tend to quicken the heart's action and raise the blood-pressure, and, therefore, excitement of every kind ought to be most studiously avoided. Even pleasurable excitement, such as seeing friends, must be strictly limited, and if friends are allowed to visit the patient they should be enjoined not to let the patient talk, but do most of the talking themselves and to avoid carefully any subject likely to lead to excitement. The great difficulty which one has often to meet with is that of keeping the patient sufficiently long in bed, because the modern treatment by salicylates lessens pain so much more quickly than the old treatment that it is much more difficult to insure prolonged rest than it used to be formerly. Caton recommends, and I think rightly, that rest should be continued for three months in order to avoid risk of relapse and consequent valvular mischief.

Clothing.—Another important point is the prevention of chills to any part of the body which would raise the tension and thus cause mischief. In order to prevent this it is customary to let patients with rheumatic fever lie between blankets instead of between cotton or linen sheets. Instead of this Caton[3] recommends a long flannel nightgown which will completely envelop the body and limbs and prevent any chance of chill. As patients suffering from rheumatic fever frequently perspire very freely, so that their nightgowns become wet and require to be changed, it is advisable to have them made to open the whole length of the back and be fastened either with tape or soft flat buttons, so that they can be adjusted or removed much more easily than when they are open in front.

A urinal and bed-pan should be used instead of a commode, which should only be employed when absolutely necessary, and then with the precautions already given (p. 236).

Sponging.—The perspiration tends to make the patients sticky and uncomfortable, and so they require to be sponged once or twice a day, or even oftener. In doing this the patient should be disturbed as little as possible, and should be exposed as little as possible, a small part of the surface being sponged at once, then dried and covered up, and the nurse should take care that the windows are shut, and that no draught should blow upon the patient during the process. It is important that the temperature of the patient should be kept as far as

possible from rising high, because the high temperature of the blood causes increased action of the heart, and this, of course, is injurious. One of the best means of keeping the temperature down is to sponge the whole body and limbs with warm water as hot as can be comfortably borne, and then instead of drying the surface simply to dab off the loose water and then cover the patient by a cradle over which is laid a single blanket. The water upon the surface of the patient's skin thus evaporates and tends to reduce the temperature without chilling him. If the temperature is very high the end of the cradle may be left uncovered, so that the air may enter more quickly and evaporation go on more rapidly. If the joints are very painful they ought to be protected by a cradle, and if they are wrapped in cotton-wool, this should be kept in place by several short bandages tied in front, and not by one long one passed round the limb.

While a hard bed is most uncomfortable and likely to give the patient pain and increased restlessness, too soft a bed is also bad, and I have seen a patient who was lying in great discomfort on a soft feather-bed obtain much comfort when he was put on a hard mattress on top of the feather-bed. This gave the requisite softness without being too yielding. Some patients object strongly to water-beds or water-pillows, both because of the difficulty of keeping these at a proper temperature and because of the discomfort they feel at the oscillation of the water on the least move-

ment. Both of these disadvantages are obviated by using air-pillows or air-beds instead of water-beds.

Diet.—During the febrile condition the diet should be chiefly milk alone, or if it is not well borne undiluted, it may be mixed with Vichy water, potash water, or soda water. If there is the least tendency to flatulence a simple solution of bicarbonate of soda or bicarbonate of potash in water may be used instead. Ten or fifteen grains of common salt have been recommended as an addition to a pint and a half of milk. The proprietary foods, of which there are a great number, may be used either along with, or alternately with milk if they are found to suit. Sometimes they tend to give rise to more flatulence than the milk alone does, but, on the other hand, they are sometimes better digested than the milk, as they have less tendency to form curds in the stomach. When the milk treatment has to be continued long, it becomes very irksome to the patient, and this can be lessened by flavouring the milk with tea, coffee, or with chocolate. The advantage of this, of course, is that it is pleasanter to the patient, but care must be taken that the admixture of these substances with the milk does not stimulate the heart too much. Rusk, biscuit, or bread with a little butter may be given along with the milk if the patient desires it, but they should be eaten slowly and well broken up in the mouth. To vary the milk, even beef-tea, mutton-tea, or chicken-tea may be given alone, or with rusk, or bread in the way just

mentioned. These meat-teas should not be strong, and if made from meat extracts with hot water they should not be more than a pale straw colour.

When the febrile condition disappears the diet may be increased, giving fish, eggs, boiled or poached or omelette, and meat jellies if the patient likes them. Care should be taken to increase the diet very gradually and at once restrict it again if the increase seems to be doing harm.

Drinks. — When there is much thirst the diluted milk is both meat and drink, and if the patient requires more liquid, perhaps there is nothing better than the old-fashioned imperial drink. There are a good many different ways of making it; the essence of it is 1 to 2 drachms of acid potassium tartrate to an imperial pint of water. This is flavoured with syrup of lemon or lemon juice or syrup or sugar only. My own preference is for the formula used at St Bartholomew's Hospital of a teaspoonful of potassium acid tartrate with half a fresh lemon and sugar to taste, boiling water 20 ozs. This should be occasionally stirred until cold and then strained.

Stimulants.—As a rule patients are better without stimulant, but if the pulse is flagging or digestion is badly performed, whisky or brandy may be given as necessary, in quantities varying from 1 to 6 ozs. in the twenty-four hours. It is best to put the quantity into a measured bottle every twenty-four hours, so that the exact amount used can be at once observed. It is best not to give a large dose at once, but rather

to give it frequently in small quantity, 1 to 2 drachms along with the milk.

Flatulence.—The effect of flatulence upon the heart is sometimes very distressing and must be avoided as far as possible. Milk does not give rise to flatulence to the same extent as carbohydrates do, and therefore if the flatulence be distressing it is advisable to put the patient, for a short time at least, upon an entirely milk diet. If solids are given at all it is best to give them separately from the liquids and allow at least an interval of an hour between them. The production of gas in the stomach and intestines may be lessened by antiseptics, and when present its expulsion may be attained by carminatives (p. 360).

Medicines.—Salicylate of soda is the remedy *par excellence* for acute rheumatism. The natural salicylate is better than the artificial. It should be given in doses of 10 to 15 grs. every four hours, or if the temperature be high and the pain great, every three hours, or even more frequently. Some patients greatly dislike the taste of it, but its somewhat sweet and mawkish taste may be disguised by a little tincture of orange peel or liquid extract of liquorice or other flavouring agents. When singing comes on in the ears the dose should be lessened or omitted once or twice altogether. If it seems to be exerting too depressing an effect upon the pulse half a drachm to a drachm of aromatic spirits of ammonia may be added to each dose, and if there are any indications of cardiac failure five to seven minims of tincture

of nux vomica or liquor strychninæ, and 5 minims of tincture of digitalis or more may be added to each dose of the salicylate. If a more rapid action is desired the thirtieth of a grain of sulphate of strychnine may be used as a hypodermic injection.

As the temperature falls and the pain subsides the dose of salicylate may be gradually lessened to 10, $7\frac{1}{2}$ or 5 grs. every six or eight hours, but it is well to keep it up in small quantities for a week or ten days after the symptoms have quite subsided, and if any indication of any relapse should occur larger and more frequent doses should be given again at once.

Elimination.—It is important that the intestinal canal should be kept clear so as to avoid any accumulation whatever, and this may be effected by some preparation of cascara or senna; but it is advisable also to stimulate the liver, and for this purpose 1 or 2 grs. of calomel may be given on alternate nights and followed by an effervescent saline in the morning. It sometimes happens that when patients are lying in bed salines do not act well, and if so, the salines must be mixed with some other purgative such as the Mistura Sennæ Composita of the Pharmacopœia.

Local Applications.—Before the introduction of salicylates the swollen and painful joints in acute rheumatism were frequently treated with the application of a strip of blister, about an inch or an inch and a half broad, round the limb, just above and below the joint, and this treatment appears to be to some extent one of serothera-

peutics because it had the effect of increasing the alkalinity of the urine.

Endocarditis.—In a case of rheumatic fever if the pulse becomes unduly quick or irregular and the temperature rises without any apparent reason endocarditis may be suspected, and dilatation or the presence of a murmur at one of the orifices should be looked for. Should this occur the precautions already mentioned regarding rest should be enforced still more rigidly, and if there is distress over the heart or palpitation, ice-bags may be employed and warm sponging over the rest of the body in the manner already described. If the ice-bag is applied directly to the skin it is apt to induce a feeling of chill, which is avoided by covering it with flannel. If the pain is acute the application of half a dozen leeches over the cardiac area is probably the best means of removing it. Dover's powder in 10 gr. doses has the double action of relieving pain and tending to lower the temperature; but if the pain is very acute, a hypodermic injection of $\frac{1}{8}$th to $\frac{1}{3}$rd of a grain of morphine will give relief more quickly. If the pulse becomes very small or irregular and the heart shows signs of rapid dilatation, digitalis may be given in doses of 5 minims every two or three hours, its action being carefully watched. If the temperature tends to rise much in spite of sponging as already recommended and the application of the ice-bag, phenacetin in doses of 3 to 10 grs. may be given, or 5 grs. of antifebrin. I think phenacetin is rather less depressing than either antipyrin or

antifebrin, and so is to be preferred, and along with it cardiac stimulants such as ether and ammonia, or strychnine, either by the mouth or subcutaneously, may be employed as seems necessary.

Pericarditis.—When a friction over the heart indicates commencing pericarditis the treatment is the same as for endocarditis. Diminution or absence of the apex beat with increased dulness, especially towards the right, indicates the beginning of pericardial effusion, and a series of small blisters about the size of a shilling should be applied over the precordial region. Four or five may be employed at once and a similar number over fresh pieces of skin after a couple of days. The pain may sometimes be removed by salicylic ionization.[4] If the effusion is not disappearing iodide of potassium in 5 or 10 gr. doses and digitalis may also be given to promote absorption and increase the action of the kidneys. Any of the preparations of digitalis may be used, but personally I have a prejudice, possibly unfounded, in favour of the infusion in doses of 1 to 2 drachms. Should the effusion continue to increase and interfere with the action of the heart, causing the pulse to become small and very quick, the breathing difficult, and the face dusky, it is advisable to remove the effusion either by aspiration or by incision. An aspirating needle may be introduced in the fourth or fifth interspace about the nipple line. Before doing this the cardiac dulness should be carefully mapped out to make sure that it is due to effusion and not simply to cardiac dilatation.

Septic Endocarditis and Pericarditis.—Although acute rheumatism is the most common cause of heart disease, yet both endocarditis and pericarditis may occur from invasion of the blood by various micro-organisms, and streptococci, pneumococci, staphylococci, gonococci, and various species of bacilli all give rise to acute heart affections.

Apparently these enter very frequently from the tonsils. In patients who suffer much from tonsillitis it is advisable to have the tonsils removed. Some of these cases are most insidious in their onset, and are only discovered almost by accident on examination of the heart after a sudden rigor or fainting fit. In such cases the treatment is absolute quiet in the manner already described, but the urine should be carefully examined for micro-organisms, and if none be found in it the secretion from the tonsils or sputum should also be examined. Failing this, the blood should be examined carefully for micro-organisms. Ten cubic centimetres are wanted at least for this purpose, and should be taken by a sterile instrument directly from the vein. Should any organisms be found, a vaccine ought to be made and injected in proper quantities, and at proper intervals, to be determined by the severity of the case. Medicines, as a rule, are of very little use, but I have seen some cases recover under the use of 15 to 20 grs. of benzoate of soda every two hours. I have also seen recoveries from oil of eucalyptus. The average dose of this is given in the United States Pharmacopœia as 1 to 8 minims. The

average given in the English textbooks is much less, but unless the larger dose is given it will be of little avail, and it may be given in emulsion with mucilage.

Treatment of Convalescence from Acute Heart Disease. — When the temperature has become quite normal and the pains are all gone, the dieting may be increased carefully by allowing a little fish, such as whiting or sole. If this agrees, haddock or cod may be given. These fish are best boiled, but if they are agreeing well the sole may be given fried, great care being taken to remove all the skin before it is eaten. The breast of chicken may then be given, and in a few days more, some minced meat may be tried, gradually proceeding to a small cutlet or slice of mutton, and later on to beef. Along with this may be given at first toast, and afterwards some potato well boiled or mashed. Green vegetables have a tendency to cause flatulence, but at the same time they are useful, both in varying the diet and having a laxative action upon the bowels. Mashed turnips, mashed carrots, spinach, cauliflower, and brussels sprouts, or asparagus, if in season. Peas, even though green and quite soft, must be carefully chewed, for there is a tendency to swallow them whole, and then they are apt to cause flatulence.

LITERATURE.

[1] Lauder Brunton, *Edin. Med. Journ.*, 1897, May 1st, 466.
[2] R. Caton, *The Prevention of Valvular Disease of the Heart* (C. J. Clay & Sons, London, 1900, p. 12).
[3] *Ibid.*, p. 35.
[4] Mackintosh, *Brit. Med. Journ.*, 1913, vol. ii., p. 1205.

CHAPTER XVII

GENERAL PRINCIPLES OF TREATMENT IN HEART DISEASE

The Heart is not an Isolated Organ—Its Efficiency Depends on Good Quality of Blood—Requirements for this — Digestion — Assimilation—Metabolism — Excretion — Mastication — Gastric Digestion — External and Internal Secretions—Autocoid Substances —Hormones — Chalones — Intestinal Digestion — Absorption and Assimilation—Autointoxication—Action of the Liver — Defecation — Metabolism — Exercise — Excretion — Bowels—Liver—Kidneys — Skin.

General Principles of Treatment in Chronic Heart Disease.—In acute heart disease the duration of the disease is brief, and the attention of the physician is directed chiefly to the organ affected; but the case is different with other forms, which may last for many years. In the treatment of such cardiac diseases whether organic or functional, it must always be borne in mind that the heart is not an isolated organ, but is part of the body, and that the nutrition, functional activity, and efficiency of the heart depend upon the condition of the blood which it has to drive through the body (*cf.* p. 151), as well as on the varying activity of

the muscular and nervous systems which it is called upon to meet. The condition of the blood again depends upon the efficiency with which the processes of digestion, assimilation, tissue-metabolism, and excretion by the bowels, kidneys, and skin are carried on. Tissue-metabolism has, undoubtedly, a great deal to do with the condition of the blood, and is especially dependent on the secretions of the ductless glands. At present our knowledge of their functions and of the action and reaction of their secretions upon each other is still very imperfect, and although we are now beginning to use the dried glands or their products as medicines in disorders of the circulation, we are still obliged, at present, to rely more upon the older remedies for promoting (1) digestion, (2) assimilation, and (3) excretion, than upon the newer ones which modify tissue change. When an inexperienced man begins driving a horse and finds that the animal is not going steadily as it usually would do, but throws its head up and down, or jerks uneasily from side to side, or sometimes goes quickly and sometimes nearly stops altogether, he is apt to pull at the reins and use the whip; while an older and more experienced man would at once ask himself, "Why does the animal do this?" He would look at the horse's mouth and see whether the bit was not hurting it, whether the harness was not fretting its skin, and whether it had not got a stone in its shoe. He would try to remove all sources of annoyance from the animal before he either pulled at the reins or

used the whip. In the same way, a young physician who is called upon to treat some irregularity of the heart is apt at once to have recourse to digitalis, strophanthus, or nux vomica and the like, but one with more experience would ask himself, "Why is this heart going irregularly?" and he would very likely find that the irregularity was due to excessive acidity in the stomach, to flatulence in the stomach or bowels, or to some imperfect action of the liver as shown by tenderness over that organ, with perhaps pale stools and a slight icteric tinge of the conjunctivæ. All these he would try to put right before having recourse to drugs which would act more powerfully upon the heart, and in most cases the result would be more satisfactory than if he had begun at once with the latter class of remedies.

Digestion.—The first part of the digestive processes is mastication, and a great many cases of dyspepsia depend either upon deficiency of teeth or the presence of decayed teeth, or on too great hurry in swallowing food, so that there is no time for proper mastication. An imperfect set of teeth is often worse than no teeth at all, because, as shown in the diagram (Fig. 107), the remaining teeth simply prevent the jaws from meeting, and there is almost no grinding surface at all. Where this is the case artificial teeth ought to be put in. When teeth are decayed they ought to be stopped if possible, as the decayed cavity forms a reservoir for microbes of all sorts, which tend to infect the food as it passes from the mouth into the

stomach. Pyorrhœa is another common cause of infection of the food, and not only so, for I have seen a case of fatal ulcerative endocarditis where I felt quite sure the infective microbes had been absorbed from the alveoli of the teeth. It is very difficult to do anything with this condition, excepting by thorough scaling of the teeth, combined with vaccine treatment, or, in very advanced cases, by extraction of the teeth. Perhaps the simplest method of treatment, which can be employed by the patient himself,

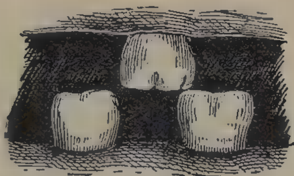


FIG. 107.—Defective teeth, showing how they may prevent the gums from meeting, without presenting any grinding surface.

is to paint the gums round at their junction with the teeth with tincture of iodine, or to wash the mouth frequently with a solution of peroxide of hydrogen. The tonsils are a common source of infection, and if there is any tendency to tonsillitis they may be painted every night, or every night and morning, with equal parts of glycerine of tannic acid and tincture of iodine. If very large and subject to frequent inflammation, they ought to be removed. Hasty mastication is an exceedingly common cause of dyspepsia, especially in busy men or in people of a nervous temperament. When these begin to think of any work that is to be done they are apt to

swallow their food without thinking what they are doing. For such people it is a good thing to follow the rule observed by the late Mr Gladstone, I believe on the advice of the late Sir Andrew Clark, to give every tooth a chance, and bite each mouthful of meat thirty-two times, counting the bites. The advantage of such thorough mastication is not only that the food is more finely comminuted, but the longer mastication causes a greater secretion of saliva. This assists digestion both directly by converting starch into sugar, and also indirectly by stimulating the secretion of gastric juice. Another aid to thorough mastication is afforded by not eating and drinking at the same time. Many people are apt to chew their food very imperfectly and wash it down with liquid, either water, tea, coffee, wine, or spirits, during the meal. When no liquid is taken with the meal, this becomes almost impossible. The food must then be broken up thoroughly and mixed with saliva.

One great rule in indigestion of all sorts, therefore, is to take little or no liquid during meals.

When liquid is drunk towards the end of a meal, the danger of imperfect mastication is lessened, but much liquid taken at this time will still interfere with digestion in the stomach, by diluting the gastric juice and so weakening its digestive power.

Of course, a large quantity of food which would distend the stomach mechanically should be avoided; and, if required, the meals should be

small in quantity and more frequently repeated. Articles of diet that tend to cause flatulency, such as cabbage, pastry, and sugar, should also be avoided, or anything else that seems to disagree with the patient.

As Pawlow[1] has shown, tasteless and unappetising food does not stimulate either insalivation or gastric secretion, whereas tasty, appetising food will do both; so the manner in which food is cooked and presented to the patient is almost, or quite, as important as the nature of the food.

It is curious to notice how often a meal of the very plainest character such as a slice of boiled mutton with a potato or piece of stale bread eaten at home will cause discomfort and pain, while a large table d'hôte dinner can be eaten with pleasure and impunity. But, while people who have a tendency to flatulence or indigestion should take little or no liquid with their meals, it is evident that as the body contains so much water, water must be taken in some form or another during the day. The best form in which to take it is that of simple hot water, as hot as can comfortably be drunk, with a slice of lemon floating on the surface to relieve the insipidity of the hot water itself. The water should not be drunk in large draughts, but should be slowly sipped. The best time for taking the water is when digestion in the stomach is finished, that is to say, three or four hours after a meal. Thus, if breakfast be taken at 8, some hot water may be sipped between 11 and 12. If lunch be taken at 1,

some hot water may be sipped between 4 and 5. At this time the water may be either sipped alone or it may be slightly flavoured with tea, or the water may be sipped first and a cup of ordinary tea drunk afterwards. The water alone is best, because the cup of tea sometimes gives rise to acidity and flatulence; but its refreshing power is so great that in some cases it may be allowed, and if so, it ought to be China tea. If hot water or tea be disliked, the water may be simply flavoured with some kind of meat extract; or thin broth, julienne soup, or beef-, mutton-, or chicken-tea may be substituted, but it must not be strong. Water should again be sipped before going to bed.

Water taken in this way not only supplies the needs of the body, but tends to wash out the contents of the stomach after each meal, so that no food is left behind to ferment. When the stomach is not cleaned out, remnants of food are apt to undergo fermentation, and the portion of each meal that is left behind tends to start fermentation in the next meal, so that a state of indigestion is set up which may remain for a length of time.

Gastric Digestion.—In the stomach, carbohydrates such as starches may still undergo a certain amount of conversion into sugar by the saliva with which they have been mixed in the mouth, but as the acid gastric juice accumulates, the action of the saliva diminishes, and in the stomach it is chiefly the digestion of proteins which occurs. The rapidity of gastric digestion does not depend only on the amount of gastric

juice or pepsin contained in it, but also upon the motor activity of the stomach by which the gastric juice is mixed up with the gastric contents. Pleasurable ideas connected with food increase the gastric juice even when no food reaches the stomach itself, while unpleasant emotions have an opposite effect.[2] Meat extracts, albumoses, and peptones, as well as bread, have a stimulating action,[3] so that the practice of beginning a meal with a small quantity of soup is physiologically correct, only the soup must not be too strong and it must not be in too large quantity.

According to some physiologists alkalies lessen the secretion of gastric juice, while acids stimulate it;[4] but this is hardly in agreement with clinical experience, because small quantities of alkali, such as 10 grs. of bicarbonate of soda, given shortly before a meal are usually more efficient than similar quantities of mineral acids in lessening dyspepsia; this is probably due to the slight irritant action of the alkalies on the stomach wall, resulting in improved circulation, and lessened pain and distension. In the case of carbonates and bicarbonates, carbonic acid is liberated, which will aid the carminative action and tend to increase the movements of the stomach. Alkalies may also help by rendering the mucus less tenacious, thus allowing the gastric juice freer access to the food. Nevertheless, small quantities of hydrochloric acid, such as 10 to 15 minims of dilute nitro-hydrochloric acid (B.P.), given after a meal, along with some preparation of pepsin, often help weak digestions very con-

siderably. A good many years ago I made a study of the comparative strengths of many kinds of commercial pepsins, and to my astonishment I found that some specimens which gave very good results clinically contained very little pepsin but a good deal of rennin.

The peristaltic movements of the stomach are stimulated by bitter infusions [5] and by carbonic acid,[6] so that the practice of giving bitters in dyspepsia is well founded. The pylorus is very sensitive to the reaction of gastric juice, thus a slight acidity on the stomach side of the pyloric ring forms the stimulus which relaxes the tone of the pylorus and allows the stomach contents to pass into the duodenum. Acidity on the duodenal side of the pylorus produces closure of the pyloric valve, so that the opening and closing of the pylorus is determined by the relative acidity of the bowel contents on its two sides; thus it is obvious that too great alkalinity or too great acidity both cause spasm of the pylorus, with retention of the contents of the stomach.[7] When retained in this way, lactic acid is apt to be formed in larger quantity by decomposition of hydrocarbons, distension becomes still greater, and finally vomiting may occur. Much acidity of the gastric juice, therefore, ought to be combated by the use of alkalies in fairly large doses. If an alkaline solution is sipped, a little at a time, there is very little fear of getting such a degree of alkalinity of the gastric contents as to cause spasm of the pylorus. In addition, however,

to chemical stimulation the pylorus reacts also to mechanical stimulation,[8] and if large pieces of food have been swallowed and remain undigested in the stomach they irritate the pylorus in their attempts to pass into the duodenum, and thus cause spasm and irritation. For example, cheese, which is a very useful food in many cases of cardiac disease, because it contains proteins without any of the soluble products of albuminous decomposition such as are contained in meat, is sometimes regarded as very indigestible. The reason of this is that cheese is very unabsorbent and the gastric juice can only attack it at its edges. If thoroughly comminuted it is digested quite readily, but if swallowed in lumps it may remain in the stomach for hours with only its corners digested, and will not pass through the pylorus. The consequence of this is that cheese taken in this way will remain until the contents of the stomach become very acid, and when vomiting occurs everything is found to be digested excepting the lumps of cheese. For this reason it is often said that "cheese digests everything but itself." It is important that this should be understood, because in cases of high tension where butcher meat is inadvisable, cheese forms a useful addition to the dietary.

Thickening of the mucous membrane by congestion, such as is apt to occur in backward flow of blood from mitral and tricuspid regurgitation, tends to lessen the size of the pylorus, as shown in the diagram, Fig. 108, and if the opening is already small the difference

caused in it by the congestion will be proportionately great. Catarrh of the mucous membrane will have a similar effect, and in addition the larger amount of mucus secreted tends to increase the acidity of the gastric contents as well as to favour fermentation. In

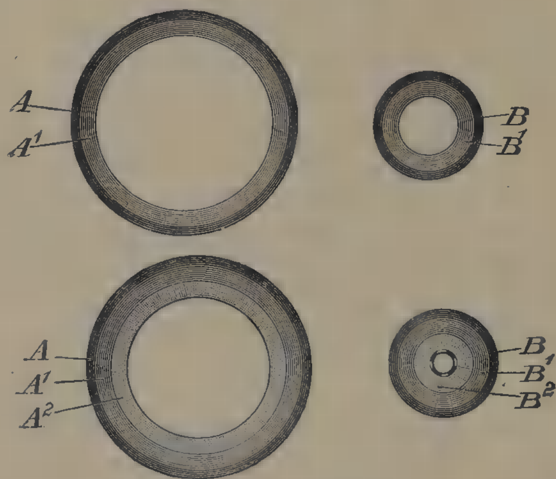


FIG. 108.—Diagram to illustrate the effect of swelling of the mucous membranes in a large and small orifice. A and B are the muscular coats. A^1 and B^1 the normal, and A^2 and B^2 the swollen mucous membranes.

such a condition preparations of bismuth along with alkalies are most useful.

Cases are by no means infrequent in which gastric catarrh and consequent dyspepsia appear to depend on post-nasal catarrh, the mucus from the nose along with the microbes it contains being constantly swallowed and so infecting the stomach. In such cases, treatment directed to the stomach alone is of little use,

and much improvement does not occur until the nose receives attention.

External and Internal Secretions.—It has been discovered of late years that physiological processes are much more complicated than they were formerly supposed to be, and that secreting glands while pouring out on a free surface an active secretion like the gastric juice, are also sending back into the blood other materials, which influence other glands or organs.

The active principles or enzymes by which complex chemical molecules like those of proteins are split up, are present in the glands or tissues in inert forms as zymogens[9] which only act when they break up and yield active enzymes. They may be likened to a pocket-knife, which is quite inactive either for good or ill until the blade is opened. Then it will cut; and an active enzyme will split up molecules. When the blade is again shut down it becomes inert; and apparently there is some provision for active enzymes again to become inert zymogens. Pepsin and acid are not present in the fasting stomach, but pepsinogen and sodium chloride are present in the deeper layers of the mucous membrane. When secretion begins, the sodium chloride splits up and forms with water hydrochloric acid,[10] while the sodium passes into the blood and increases its alkalinity so that urine secreted at the height of gastric digestion is usually neutral or alkaline, sometimes so much so that it is actually milky when passed, from the precipitation of alkaline phosphates in the bladder.[11] When the acid chyme passes into

the intestine, the acid is absorbed and the alkalinity of the blood and urine lessened, but in cases of pyloric stenosis the alkalinity of the urine may be more or less persistent.

The pepsinogen also breaks up and pepsin is secreted into the stomach.[12] At the same time

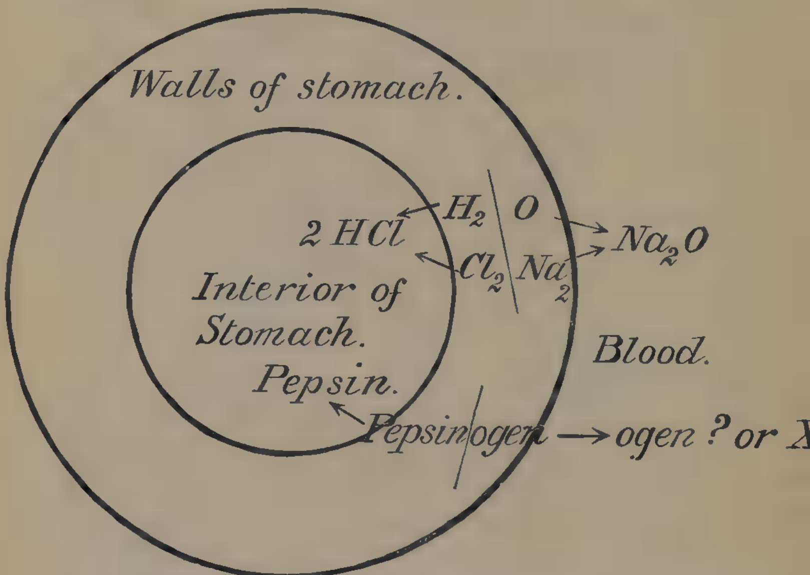


Fig. 109.—Diagram to illustrate the chemical changes in the stomach during secretion.

it is probable that something which I have marked in the diagram, Fig. 109, as X, is returned into the general circulation and acts on other glands.[13]

We do not, at present, know exactly what X is in the case of the stomach, but in the case of the intestine, while intestinal juice is poured out

into the gut, a body called "secretin" is sent into the blood, which, going to the pancreas, stimulates it to secrete.[14] Such substances, which pass from one gland into the blood and activate the zymogens in another, are called hormones (ὁρμάω, to excite).[15] But they have not all an exciting action, for some check instead of activating. For these the name of chalones has been proposed (χαλάω, to relax).[16]

The name "autocoid substances" has been suggested to include both hormones and chalones.[17]

As the action of one organ is thus so closely united with that of others, it is very evident how necessary it is to attend to all organs as far as possible and not to confine the attention to one alone, even though that organ be such an important one as the heart.

Intestinal Digestion.—When the acid chyme enters the intestine from the stomach it stimulates the mucous membrane to secrete, and while the intestinal glands are pouring a digestive fluid into the bowel they are sending into the blood hormones which stimulate the pancreatic secretion, which, being poured out into the duodenum, finishes the digestion of proteins begun in the stomach and effects that of carbohydrates and fats.[18]

Absorption and Assimilation.—Absorption is chiefly effected in the large intestine, and it does not consist in a mere passage of soluble substances from the intestinal cavity into the blood-vessels and lymphatics of the intestinal wall. For protein substances such as albumins

which are in themselves innocuous, are split up by digestion into simpler molecules, the albumoses, which are powerful poisons and rapidly cause death if injected directly into the veins. But during absorption by the intestine synthetic processes appear to occur by which the poisonous albumoses are again built up into innocuous albumins before reaching the blood.[19]

Autointoxication.—The process of disintegration of proteins in the intestine does not always stop at albumoses, for part of them is still further broken up, either by the digestive juices or by microbes present in the intestine, into amino-acids and toxamines—bodies allied to ammonia in their chemical nature, and very poisonous.[20] Some of them act on the heart and vessels, and may not only raise the general blood-pressure but may produce many symptoms of cardiac or vascular disorder which are purely due to autointoxication and not to any organic disease.[21]

When the intestinal contents remain a long time in the bowel before evacuation, greater opportunity is afforded for the production of poisons by microbes, and thus a regular action of the bowels is very desirable.

Action of the Liver.—The danger of disease or death from autointoxication is greatly lessened by the liver, through which all the blood from the intestines must pass before it reaches the general circulation. The liver prevents the organism from being flooded with the large amount of sugar which starchy food

yields by converting it into glycogen and storing it up for a while, again pouring it out as needed. But the liver also seems to have the power of converting urates into urea, for Stockvis [22] observed that the pulp of a liver taken during digestion has this power, though that of a fasting liver has not. These experiments were repeated and confirmed by Brunton and Bokenham [23] and by Wiener.[24] When this function is imperfectly performed, urates will appear in the urine.

In addition to these functions which are related to the ordinary digestion of food, the liver prevents the passage of poisons from the portal into the systemic circulation. Some of these poisons it actually destroys; [25] others it catches on their way from the portal vein to the vena cava and secretes them into the bile, in which they are again sent back into the duodenum.[26]

Here they may either be swept on with the intestinal contents, and excreted with the fæces, or they may undergo reabsorption and pass again to the liver. They may thus go round and round in the enterohepatic circulation for a long time without producing much effect (Fig. 105), until they are either removed by a purgative, or accumulate so much that the liver can no longer deal with them, and they, therefore, enter the general circulation and produce toxic symptoms. Bile is secreted under very low pressure, and the chief agent in its expulsion from the liver is the pressure to which that organ is subjected by the diaphragm and

abdominal walls.[27] In simple walking this pressure is so slight that the liver is not squeezed at all, and the bile tends to remain in the ducts. But in climbing a steep ascent, or in bending forwards to touch the toes, when the diaphragm is depressed by a full inspiration, the liver is squeezed, the bile evacuated from it, and by a course of such exercises many of the symptoms known as "biliousness" may be removed.

When the patient is too feeble for exercises considerable benefit may be obtained by proper massage of the liver.

Defecation.—In cases of cardiac disease it is frequently of the greatest importance to avoid straining at stool. I have elsewhere* pointed out that the anus is in front of the axis of the pelvis, and the expulsive efforts tend to drive the fæcal mass against the pelvic floor just under the coccyx. When this point is supported mechanically the expulsion of a large fæcal mass is greatly expedited. Usually it is better by diet and laxatives to keep the motions soft, and if this is insufficient the bowel should be washed out by an enema rather than allow any strain which may produce serious or even fatal consequences (*cf.* p. 172).

Metabolism. Exercise.—We have already seen how the activity of one gland promotes that of another, and the internal secretions of the thyroid[28] and pituitary[29] glands affect, to an enormous extent, the growth and development

* *Disorders of Assimilation* (London: Macmillan & Co.), 1901, p. 231.

of the body generally. Every organ during its functional activity seems to produce substances which are useful to other organs, but which if retained in it are poisonous to itself.[30] A free flow of blood through the organ is, therefore, necessary not only for the supply of fresh food materials and of hormones, but also for the removal of waste products. Claude Bernard[31] showed that when the submaxillary gland is made to secrete by stimulation of the chorda tympani nerve, the afferent artery to the gland dilates at the same time; and Ludwig and Sadler[32] showed that when muscles are stimulated to contraction their arteries dilate so that more blood passes through them. Exercise of the muscles, therefore, supplies them with blood, increases their contractile power, and maintains their nutrition, whereas muscles which are not exercised at all become soft and flabby, and lose their power of contraction to a great extent. The heart is a muscle and is subject to the same laws of nutrition as the other muscles. While the feeble heart is to be protected from over strain, its nutrition is improved by moderate exercise, and absolute inactivity, where this is not required, is bad for the patient's heart as well as for his general condition.

As I have already mentioned (p. 237), where the patient is unable to take exercise its place may be supplied to some extent by systematic massage.

Excretion.—The removal of the waste products formed by each organ during its functional activity is effected by the blood and lymph

which pass from it, but unless these are more or less constantly removed from the blood it will gradually become overcharged with them, and will lose its vivifying power. Attention to the due performance of their functions by the excretory organs—bowels, liver, kidneys, and skin—is thus essential to the welfare of the patient. The necessity for water has been already mentioned, but there are great differences between patients in the amount of water they naturally take, for while some are liable to feel thirsty and drink water freely, others take so little that their motions are hard, their bile scanty, their skin dry, and their urine scanty and concentrated. In such cases the necessity for more water must be insisted upon, and a minimum quantity prescribed. The eliminating organs must be stimulated as required by laxatives, hepatic stimulants, diaphoretics, and diuretics.

LITERATURE.

[1] Pawlow, *The Work of the Digestive Glands*, trans. by W. H. Thompson, 2nd ed., 1910 (London : Griffin & Co.), pp. 52, 95 ; see also Pawlow and Schumowa-Simanovskaia, *Zentralb. f. Physiol.*, 1889, vol. iii., p. 113; *Arch. f. Anat. u. Physiol.*, 1895, p. 53; Chischin, *Inaug. Diss.*, 1894 (St Petersburg) ; cf. *Jahresb. ü. d. Fortschr. d. Thier Chemie*, 1895, Bd. xxiv., p. 347 ; Bidder and Schmidt, *Die Verdauungssäfte und der Stoffwechsel*, 1852 (Leipzig) ; Richet, *Le Suc gastrique chez l'homme et les animaux*, 1878 (Paris), p. 153.

[2] Pawlow, *op. cit.*, p. 103.
[3] Pawlow, *op. cit.*, pp. 116-19; Schiff, *Lecons sur la Physiologie de la Digestion*, 1867, tome ii., p. 205; Chischin, *op. cit.;* Edkins, *Journ. of Physiol.*, 1906, vol. xxxiv., p. 139.
[4] Pawlow, *op. cit.*, pp. 232, 244.
[5] Batelli, *Dissert.*, 1896 (Genf).
[6] Schierbeck, *Skand. Arch. f. Physiol.*, 1891, Bd. iii.; Meyer and Gottlieb, *Exper. Pharmakologie*, 1910, p. 159.
[7] Cannon, *Mechanical Factors of Digestion*, 1911 (London: Arnold), p. 96 *et seq.;* Moritz, *Verhandl. d. deut. Naturforscher und Aerzte*, 1893, p. 25.
[8] Cannon, *Amer. Journ. of Physiol.*, 1898, vol. i., p. 369; Cohnheim, *Münch. Med. Wochenschr.*, 1907, vol. liv., p. 2582.
[9] Heidenhain, *Arch. f. d. ges. Physiol.*, 1875, Bd. x., p. 581 *et seq.;* Langley, *Journ. of Physiol.*, 1882, vol. iii., p. 269; Moore, *Recent Advances in Physiol.*, edit. by L. Hill, 1908 (London: Arnold), pp. 108-9.
[10] Voit, *Sitzungsber. d. k.-bayer. Akad. d. Wissensch. zu München.*, 1869, Bd. ii., p. 483; Cahn, *Zeitschr. f. physiol. Chem.*, 1886, Bd. x., p. 522; Grüber, *Beitr. z. Physiol.* (C. Ludwig, *z. s. Geburtstag gewid.*), 1887; for theories of origin, *vide* Schäfer's *Textbook of Physiol.*, 1898, vol. i., pp. 360-3.
[11] Maly, *Ann. d. Chem.*, 1874, Bd. clxxiii., p. 232; Quincke, *Jahresb. ü. d. Fortschr. d. Thier Chemie*, 1874, Bd. iv., p. 241; Stein, *ibid.*, 1876, Bd. vi., p. 161.
[12] Grützner, *Arch. f. d. ges. Physiol.*, 1878, Bd. xvi., p. 105; Langley, *Journ. of Physiol.*, 1882, vol. iii., p. 278 *et seq.*
[13] Edkins, *Journ. of Physiol.*, 1906, vol. xxxiv., p. 133; Starling, *Recent Advances in Physiol. of Digestion*, 1906 (London: Constable), p. 75.
[14] Bayliss and Starling, *Journ. of Physiol.*, 1902, vol. xxviii., p. 325.
[15] Starling, *Recent Advances in Physiol. of Digestion*, 1906 (London: Constable), p. 90; Bayliss, *Nature of Enzyme Action*, 1908 (London: Longmans, Green).
[16] W. R. Hardie, *vide* Schäfer, *Brit. Med. Journ.*, 1913, vol. ii., p. 380.

[17] Schäfer, Physiol. Section, XVII. Internat. Congress of Medicine, London, *Brit. Med. Journ.*, 1913, vol. ii., p. 380.
[18] Starling, *op. cit.*, p. 88.
[19] For fuller information, *vide* Lauder Brunton, *Introd. to Modern Therapeutics*, 1892 (London: Macmillan & Co.), p. 46; v. Noorden, *Metabolism and Practical Medicine*, edit. by I. Walker Hall, 1907 (London: Heinemann), vol. i., pp. 15, 64.
[20] Moore, *Schäfer's Textbook of Physiol.*, 1898, vol. i., p. 421 *et seq.*; Abderhalden, *Zeitschr. f. physiol. Chemie*, 1905, vol. xliv., p. 17; v. Noorden, *op. cit.*, vol. i., pp. 9, 13.
[21] Albertoni, *Centralbl. f. d. med. Wissensch.*, 1880, vol. xviii., p. 577; Schmidt-Mühlheim, *Arch. f. Anat. u. Physiol. Phys. Abt.*, 1880, p. 45; Lauder Brunton, *Disorders of Digestion*, 1888, pp. 247, 284; ibid., *Introd. to Modern Therapeutics*, 1892, pp. 48, 55, 57.
[22] Stockvis, *Donder's Archiv*, 1860, p. 260.
[23] Brunton and Bokenham, *Archiv d. Sciences Biolog. de St Petersbourg*, tome xi., Supplement, Pawlow's "Festschrift," 1904.
[24] Wiener, *Zentralbl. f. Physiol.*, 28th Jan. 1905, p. 690; *cf.* Lauder Brunton, *ibid.*, 1905, Bd. xix., No. 1.
[25] Roger, *Action du Foie sur les Poisons*, 1887 (Paris); Lauder Brunton, *Disorders of Digestion*, 1888, pp. 17, 35; Rothberger u. Winterberg, *Arch. intern. de Pharmacodyn.*, 1905, Bd. xv.; Dilling, *Biochem. Journ.*, 1909, vol. iv., p. 293.
[26] Lussana, *Lo Sperimentale*, 1872, tome xxix.; Lauder Brunton, *Disorders of Digestion*, 1888, p. 201; Langer, *Zeitschr. f. exper. Path. u. Ther.*, 1906, Bd. iii.
[27] Hermann's *Handbuch d. Physiol.*, 1883 (Leipzig: Vogel), Bd. v., Theil i., p. 270; Noël Paton, *Schäfer's Textbook of Physiol.*, 1898, vol. i., p. 567.
[28] Schäfer, *Schäfer's Textbook of Physiol.*, 1898, vol. i., p. 937; Pembrey, *Recent Advances in Physiol.*, 1908, p. 575.
[29] Oliver and Schäfer, *Journ. of Physiol.*, 1895, vol. xviii., p. 277; Dale, *Biochem. Journ.*, 1909, vol. iv., p. 427; Mackenzie, *Quart. Journ. of exper. Physiol.*, 1911,

vol. iv., p. 305; Pick, *Deut. med. Wochenschr.*, 1911, pp. 1930, 1978, 2086; Wiggers, *Amer. Journ. Med. Sciences*, 1911, vol. cxli., p. 502; Cushing, *Pituitary Body and its Disorders*, 1912 (Lippincott).

30 For literature, *vide* Swale Vincent, *Internal Secretions and the Ductless Glands*, 1912 (London: Arnold); Biedl., *Internal Secretory Organs*, trans. by L. Forster, 1912 (London: J. Bale, Sons, & Danielsson); Martindale and Westcott, *Extra Pharmacopœia*, 1912, 15th ed., vol. i., p. 943 *et seq.*

31 Claude Bernard, *Journ. de la Physiol.*, 1858, vol. i., pp. 233, 649; v. Frey, *Ludwig's Arbeiten*, 1876, Bd. xi., p. 89; Langley, *Journ. of Physiol.*, 1889, vol. x., p. 316.

32 Ludwig and Sadler, *Ludwig's Arbeiten*, iv[te] Jahrg. for 1869 (Leipzig: Hirzel, 1870), p. 77.

CHAPTER XVIII

TREATMENT OF CHRONIC VALVULAR DISEASE

Aortic Stenosis—Aortic Regurgitation—Mitral Stenosis —Mitral Regurgitation.

Treatment of Chronic Heart Disease. Aortic Stenosis.—When the aortic orifice is contracted it presents more resistance to the action of the ventricle, which therefore undergoes compensatory hypertrophy. When this is complete the condition may cause no symptoms, and the only treatment required is to prevent overstrain or over-excitement of the heart by severe physical exertion, worry or stimulants, and to prevent toxæmia of any kind, either from over-eating, constipation, or microbic invasion. When compensation is perfect the patient may present no abnormal symptoms for a long time, and the condition is only recognised by a systolic bruit over the aorta. But whenever the heart begins to fail, the nervous system begins to show symptoms of imperfect blood supply, in the form of giddiness, faintness on rising, flashes of light before the eyes, and headache. Very often these are the first indications of anything wrong. Then oppression over the chest and cardiac pain may appear. This pain may be

only a dull ache coming on with exertion or excitement, or it may become intense in the form of angina pectoris.

As these symptoms indicate that the heart is no longer able to meet the calls upon it, it is necessary to lessen the work that it has got to do by lowering the tension as a whole, and preventing any undue rise at any time from bodily exercise or mental emotion. The tension must be lowered generally by prohibiting the use of red meat and meat extracts, by free elimination from the liver, kidneys and bowels, by the administration of vaso-dilators, and the use of Nauheim baths and by lessening any irritability present by nervous sedatives. So long as the mitral valves remain competent there may be very little or no shortness of breath, but as soon as the ventricle begins to yield and the valves become incompetent (Fig. 24, p. 75), then signs of pulmonary congestion and venous stasis appear.

Aortic Regurgitation.—In this condition also there may be few or no symptoms so long as compensation is perfect, and it may only be recognised by a diastolic bruit. And here I think I ought to give a word of caution as to the place where the aortic regurgitant murmur is heard. It is usually heard quite markedly over the aortic valves, or perhaps I ought to say rather over the aortic cartilage, and is propagated down the sternum, but sometimes it is not heard at all at the base of the heart, and is only audible at the lower end of the sternum, more especially to its left side. Not infrequently the presence

of aortic regurgitation is apparent even to onlookers by the curious pallor of the face, and by visible locomotion in the temporal and carotid arteries.

Persons suffering from aortic regurgitation are more liable to sudden death than those suffering from any other form of cardiac disease, except, perhaps, those who have angina pectoris. It is therefore advisable for the patient always to carry about with him a calling card or pocket-book stamped with his address, so as to insure his identification in case of death away from home. So long as the valvular lesion is fully compensated, it is not advisable to lay the patients up. All that is necessary is to warn them against sudden strain, undue fatigue, or great excitement. Many of them might walk 25 miles in a day without harm, or even with positive advantage, but 20 yards sudden spurt to catch a train might prove fatal.

The most important point in treatment is to keep the heart in good condition.

For this purpose courses of Nauheim baths and graduated resistance exercises are sometimes very beneficial.[1] In this form of heart disease the difference between systolic and diastolic pressure is greater than in any other. In the diastole the blood flows back into the heart as well as onwards into the vessels. There is thus a tendency for the diastolic pressure to sink low, and if it should sink too low it might give rise to syncope, possibly fatal.

The longer the diastole lasts the lower does the pressure fall, and, therefore, if the pulse has

been rendered slow by digitalis, greater care than usual must be taken to avoid bringing on syncope by suddenly rising from the recumbent to the upright position, in which the blood tends to flow quickly back into the heart and leave the brain anæmic (Fig. 110).

A special danger occurs under these circum-

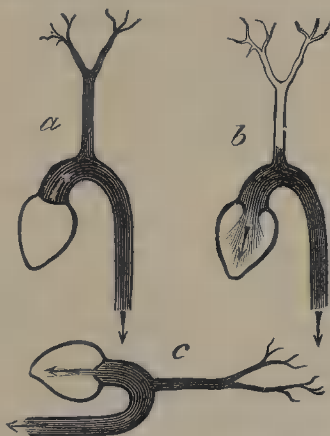


FIG. 110.—Diagram to illustrate the occurrence of syncope in cases of aortic regurgitation. In *a* the normal heart with full carotid and free supply of blood to the brain is represented; in *b* the carotid is shown empty, so that syncope will occur from blood flowing back into the ventricle as well as onward into the aorta; in *c* is shown aortic regurgitation in the recumbent posture, so that the carotid is well filled and regurgitation into the heart is rather less.

stances if the patient suddenly rises to pass water, because as the bladder is emptied the pressure on the abdominal vessels is lessened, and thus the blood-pressure tends to fall.

To prevent the diastolic pressure falling too much the arterioles or capillaries tend to contract, but this contraction may give rise also to very high tension during the systole, because the

ventricle contains a large quantity of blood which has come to it partly from the auricles and partly has regurgitated from the aorta, and it has to drive this onward against the resistance opposed by contracted vessels. The ventricle tends to yield before the strain and thus dilatation occurs. The two indications for treatment, therefore, are, firstly, to prevent dilatation by increasing the cardiac nutrition; and, secondly, to prevent too great systolic strain by dilating the capillaries. Some interesting results were obtained experimentally by Cloetta,[2] who produced aortic regurgitation experimentally in rabbits. To some of these he gave no medicine, and in them the heart became greatly hypertrophied, but they lost strength and endurance. When treated with digitalis immediately after the lesion, and for a year afterwards, the hypertrophy was much less, but the heart was almost as strong as that of a normal rabbit. These experiments seem to show that small doses of digitalis, such as 5 minims of the tincture three times a day, if given continuously as soon as the lesion is detected, kept up for some months, and again resumed when the slightest tendency to dilatation appears, may be very useful by preventing the ventricle from yielding, and thus maintaining the patient's health. Digitalis may be combined with strychnine or caffeine, and if it tends to raise the tension much a vaso-dilator, such as nitrite of soda, may be given with it. If given by itself in such doses as to raise the tension, digitalis may evidently be harmful by increasing the strain upon the ventricle, and, if it should cause much slowness

of the pulse, the tension during the prolonged diastole may fall so far as to produce fatal syncope. Instead of digitalis, strophanthus may be employed. Giddiness, palpitation, cardiac pain, or angina must be treated as they occur.

Although sudden death occurs not infrequently in aortic regurgitation, yet perhaps a still more frequent course of the disease is for the left ventricle to yield before the strain, and then the mitral valves become incompetent, so that we get all the consequences which I have previously described from backward pressure on the lungs and right heart. When this occurs it must be treated like a case of severe mitral disease.

Mitral Stenosis.—If this is present only to a very slight extent it may not interfere with the action of the heart, even although there be a pre-systolic murmur characteristic of its presence, but if the obstruction be great it produces much congestion of the pulmonary circulation with breathlessness, cough, and frequently hæmoptysis. In very many cases the valves not only obstruct the onward flow of the blood but also tend to allow free regurgitation. Mitral obstruction is much more difficult to treat than mitral regurgitation because in regurgitation benefit can be obtained by strengthening the heart, and thus not only increasing the onward flow but lessening the backward flow by contracting the mitral orifice (Fig. 24, p. 75). In mitral obstruction the interference with the circulation cannot be removed by drugs, although it may be somewhat ameliorated. Some patients are absolutely condemned to inaction, and so trying is the con-

dition, that a good many years ago I suggested[3] that it might be possible to divide the contracted valves, and thus convert the constriction into pure regurgitation. I had begun to make experiments on the subject, but a very severe illness, lasting more or less two years, prevented me from continuing them.

Mitral Regurgitation.—The treatment of mitral regurgitation depends very much upon the extent of the lesion. It is much more frequent than it is usually thought to be, and a great number of people go about with a slight mitral leakage which is never suspected until by chance they are found, on medical examination, to have a murmur indicating mitral regurgitation. They have no symptoms, they feel quite well and are able to go through a very considerable amount of fatigue. Some patients have had their lives ruined by being told that they must throw up their professions and give themselves up to a life of invalidism, taking no exercise lest they should further damage their heart. Sometimes such advice is given but not taken, and I well remember the case of a doctor who had taken his degree shortly before the Crimean War. After medical examination he had been told that he had bad mitral regurgitation, that he had not two years to live, and that he must be careful to avoid exertion of any sort. As his life was going to be so short at any rate, my friend decided that it did not much matter what he did, and he accordingly volunteered to go out to the Crimean War. He served through it, then through the

Indian Mutiny, and lived as a healthy man till between sixty and seventy years of age. In cases of mitral regurgitation it is not so much the physical signs that are to be taken into account in regarding the patient's life, as the effect of the lesion upon the patient's condition, and this may to some extent be ascertained by noting the effect upon his pulse and respiration of running upstairs or, as in the observations of Tait Mackenzie,[4] by imitating the movement of quick running without moving from the spot.

Patients having slight mitral regurgitation are usually told, and rightly so, not that they have any disease of their heart, but that it is a little weak and they must avoid straining it.

As a general rule this is all that is necessary, but when shortness of breath or symptoms of venous stasis set in, more active treatment is required, and here digitalis, strophanthus, and their congeners have their proper place. For such cases the baths and exercises known as the Nauheim treatment (p. 243) are useful. If practicable, a course at Nauheim is, I think, preferable to one at home, not only because all the arrangements of the place are suited to the treatment of heart disease, but also because patients can get there the mental and bodily rest which is so essential to a cure, and which is often difficult to get at home.

LITERATURE.

[1] L. T. Thorne, *Nauheim Treatment of Diseases of Heart and Circulation*, 3rd ed., 1909 (London: Balliere, Tindall & Cox).

[2] Cloetta, *Arch. f. exper. Path. u. Pharm.*, 1908, Bd. lix., p. 209.

[3] Lauder Brunton, *Lancet*, 1902, vol. i., p. 352.

[4] Tait Mackenzie, *Amer. Journ. of Med. Sciences*, 1913, vol. cxliv., p. 69.

CHAPTER XIX

TREATMENT OF SYMPTOMS AND FUNCTIONAL DISEASES

Treatment of Symptoms occurring in Heart Disease and of Functional Diseases of the Heart—Palpitation — Effect of Hot Baths — Graves's Disease — Tachycardia from Strain—Paroxysmal Tachycardia —Bradycardia—Stokes-Adams Disease—Faintness and Fainting—Giddiness—Shock—Sleeplessness—Causes and Treatment—Hypnotics — Intermittent and Irregular Pulse—Cardiac Pain—Treatment of an attack of Angina Pectoris—Diet and Regimen in Angina — Angina Abdominis — Cardiac Asthma—Treatment of Headache — Flushes of Heat and Morbid Blushing—Raynaud's Disease—Chilblains —Chronic Urticaria—Low Tension—High Arterial Tension—Treatment of Senile Conditions of the Vessels—Cerebral Hæmorrhage—Cerebral Thrombosis.

Palpitation.—Palpitation may occur in cases of organic disease of the heart, but it happens even more frequently as a functional condition, and in any case the first thing to do is to find out upon what it depends and remove the cause. In cases where it depends upon excessive use of tobacco, tea, coffee, or alcohol, these articles should be diminished or cut off entirely. Even in cases of organic heart disease, while it may

be impossible to cure the lesion it may be possible to relieve the symptoms, for it may depend upon causes apart from the actual cardiac disease. Sometimes it depends upon posture, and patients who do not suffer from it in the upright position may get it on lying down. If they lie down on their left side, the cardiac apex comes near to the chest wall and may impinge upon it (p. 176).[1] Each time it strikes the ribs the effect upon the heart is the same as if the ventricle were struck by the ribs, and then the action is excited and may even become irregular. When they lie upon their right side the heart tends to fall away from the chest wall and rest upon the cushion formed by the right lung, so that many people can lie upon the right side when they cannot lie upon the left. In some cases they are obliged to lie upon their backs, and this often seems to disturb the circulation to such an extent as to cause a nightmare. Often this is of such a kind as to indicate interference with the circulation through the lungs, because the dream which makes the patient awaken is that of being chased by an animal or subjected to some other sudden strain, and when he does awake he has the same sensation of oppression, and his heart is beating just as if he had been running away from a mad bull or undergoing some other violent exertion.

When palpitation depends upon distension of the stomach by flatulence pushing the heart up,[2] and thus bringing its apex against the chest wall, immediate relief is afforded by carminatives which cause expulsion of flatus (p. 225).

When palpitation is very severe it may sometimes be relieved by the application of cold to the chest by means of an ice-bag or coils of india-rubber tubing through which cold water is passed. To avoid chill it is advisable to envelop the ice-bag in flannel before applying it to the chest. I have seen the application of stimulating liniments over the cardiac region bring on palpitation, but gentle pressure by the hand over this region tends to quiet the heart. Continued gentle pressure by the application of a plaster has a somewhat similar effect, and a belladonna plaster appears to have more or less of a specific action and to be better than simple adhesive plaster (p. 263).

When the tension is high it should be lowered by the administration of nitro-glycerine or some other vaso-dilator, and small doses of digitalis or strophanthus given at the same time tend to steady the heart and thus give relief. If there is any mental excitement (*cf.* Fig. 54, p. 164) and irritation, the bromides of potassium and sodium or ammonium [3] may be given, usually in fairly large doses, such as 20 or 30 grs. at a time. Their taste is well covered by saccharin. Thus 6 to 10 grs. of each of the three bromides just mentioned may be given along with 5 or 10 minims of a 1 per cent. solution of saccharin and half a drachm or a drachm of tincture of lemon in half an ounce mixture. If this is taken in half a tumbler of soda water the taste is not disagreeable.

Palpitation is very apt to be associated with some disturbance in the pelvic organs, and any-

thing wrong with these ought to be attended to, any local lesion treated, and any excitement of them carefully avoided.

In such cases valerian is useful, and a very good prescription is the following, which I owe to the late Sir John Russell Reynolds:—

℞ Tinct. Valerian	. .	ʒj.
Tinct. Lavand. Co.	. .	♏xx.
Spt. Vin. Rect. ad.	. .	ʒij.
Mitte ℥iv.		

Sig. Two fluid drachms measured in a glass measure to be taken in one fluid ounce of water.

The object of measuring the medicine in this way is to ensure exactitude in the quantity taken. It may be used at bedtime to prevent palpitation coming on and to bring on sleep, and may also be given at other times for palpitation, but should not be used too freely, as it may induce a craving just like other forms of alcohol.

In cases where palpitation is associated with anæmia this condition must be treated by preparations of iron, either alone or with arsenic. When there is much debility, strychnine or nux vomica is of great service, and may be given as in the prescription for the "pulvis mirabilis" (p. 439), shortly before or after meals. Its action is complex, because it affects the whole nervous system, stimulating the brain, the medulla, and the heart. In most cases it can be borne even in large doses, but there are some where it does harm rather than good, more especially in patients of a highly nervous temperament, and where there is a tendency to excessive sensibility of the sexual organs.

Effect of Hot Baths.—The effect of heat is to dilate the blood-vessels (p. 92) and at the same time to stimulate the heart. Hot baths are therefore to be avoided by persons liable to palpitation, as they may bring on an attack.

Graves's Disease.—In Graves's disease we frequently meet with very considerable palpitation, associated with excessive rapidity of the heart, and sometimes we find these conditions present without any protrusion of the eyeballs. As I mentioned before (p. 165), palpitation may be caused by a too prolonged administration of thyroid gland. The best treatment for Graves's disease is undoubtedly prolonged rest in bed, and one of the most successful cases I ever had was a lady who, luckily, became pregnant shortly after the onset of the disease. She was kept constantly in bed for nine months, and made a perfect recovery.

Sometimes both the palpitation and tachycardia which occur in this disease are relieved for a time by cold over the heart. Where rest in bed cannot be borne gentle exercise may be allowed, especially in the open air, but should not be carried to the extent of fatigue. The patient must be kept free from exhaustion or strain, and anything likely to cause excitement should be avoided. The diet should be of an ordinary mixed character, and tea, coffee, alcohol and tobacco should be omitted altogether or used very sparingly. Common salt, in drachm doses, three times a day, with plenty of water, sometimes appears to be useful, and I think I have seen distinct benefit from the administra-

tion of calcium chloride in 5 to 10 gr. doses three times a day. This may be given either in milk or with chloroform water or saccharin, which disguises the taste. Kocher[4] recommends the free administration of phosphates.

As such patients are usually very emotional, bromides of potassium, sodium, ammonium, or strontium, either singly or combined, are often beneficial, quieting the nervous irritability and removing the restlessness and sleeplessness which sometimes are present.[5]

Valerian may also be used, either alone, in the manner just recommended, or along with bromides. Digitalis and its congeners have been very largely tried but the result is somewhat disappointing. Belladonna in doses of 5 to 10 minims of the tincture is sometimes useful. Suprarenal gland has an antagonistic action to that of thyroid, and I have seen benefit from its administration. It may be given in the form of a solution of adrenalin chloride in doses of 1 to 30 minims of a 1 per 1000 solution three times a day, or hemisine tabloids, beginning with the third of a milligramme, three times a day.

If the patient is able to take exercise, a moderate amount of gentle exercise in the open air is advisable; and where the patient seems too weak for much exercise, massage may take its place to a considerable extent. If other means fail and the palpitation is very distressing, the patient may be put to bed and kept there steadily—regular Weir-Mitchell treatment,[6] in fact, being adopted.

The serum, the dried blood, and the dried

milk of thyroidectomised animals have been used, and in some cases with good results. The anti-thyroid serum may be given in 5 minim doses, increased to 30 thrice daily; the dried blood in 5 gr. capsules three times a day, and the dried milk, with milk sugar to improve its keeping qualities, in doses of 5 to 10 grammes daily; in some cases as much as 30 grammes have been given. The administration of pancreatic ferment at the same time as anti-thyroid serum has been recommended on the theory that the pancreatic ferment acts as a hormone to the anti-thyroid serum and increases its activity.

Tachycardia from Strain.—Excessive exercise appears to be followed sometimes by a rapid action of the heart, which, instead of ceasing after the exercise is over, may continue for days or even weeks. In all probability such cases are due to a certain amount of cardiac strain, and ought to be treated as such.

Paroxysmal Tachycardia.—In paroxysmal tachycardia, the beats of the heart, which may previously have been perfectly normal, suddenly become excessively rapid, as much as three or four times as quick as before. It would almost seem in these cases as if each cavity of the heart were capable of giving an independent stimulus to the contraction of the whole, so that a pulse of 60 might suddenly jump up to a pulse of 240. We do not know the pathology of such cases,[7] but they are not infrequently associated with a certain amount of fatty degeneration in the heart. They are benefited during the attack by

cold applications over the heart, sometimes by drinking iced water, so as to get the effect of cold directly upon the heart through the stomach, and sometimes by a powerful stimulant, such as strong coffee. The attack may sometimes be

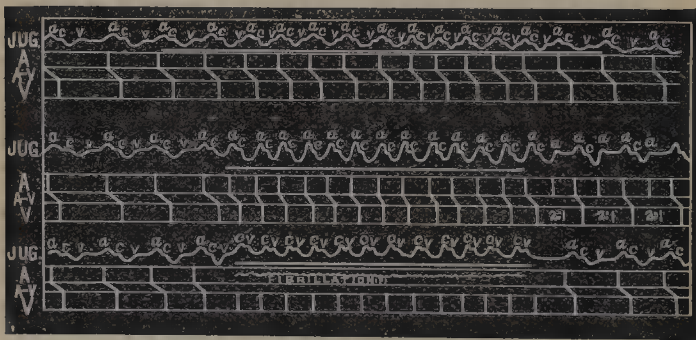


FIG. 111.—Diagrammatic method of showing the time-relations of the pulses and contractions of different parts of the heart to each other in tachycardia. JUG is the pulse in the jugular vein, A is the auricular impulse, V the ventricular impulse, A-V the time of auriculo-ventricular conduction. Its greater or less obliquity shows the greater or less time required for the transmission of an impulse from the auricle to the ventricle. *a* auricular wave. *c* carotid wave = beginning of ventricular systole. *v* end of ventricular systole. The diagram shows various types of tachycardia.

The upper line I. represents simple non-paroxysmal tachycardia showing the gradual increase and gradual decrease in rate.

The middle line II. represents paroxysmal tachycardia with persistent auricular contraction and ending in auriculo-ventricular heart-block.

The lower line represents paroxysmal tachycardia with auricular fibrillations and ventricular type of venous pulse. (After Hirschfelder.[8])

cut short by the administration of an emetic, such as 20 grs. of sulphate of zinc, or mustard and water may be employed. During the interval, small doses of strophanthus, digitalis, strychnine, and eserine may be useful in steadying the heart. If they are associated with high tension, vascular

dilators must be employed; and if they occur in gouty people, the diet should be, to a great extent, non-nitrogenous. In some cases the attack of tachycardia appears to be due to reflex irritation from the stomach, and bismuth, sodium bicarbonate, pepsin, or other digestive ferments are of service by lessening dyspepsia, while bromides diminish reflex irritability, and dilute hydrocyanic acid acts as a local gastric sedative. The attacks may sometimes be cut short by stimulation of the vagus, either directly by compression or reflexly, *e.g.* :—

Dr Augustus Waller[9] found that the best way to compress the vagus is to press the thumb over the carotid close to the angle of the lower jaw and for a short distance above and below, the fingers being placed at the back of the neck. This pressure slows the pulse, weakens it, and may render it irregular. This condition is accompanied by uneasiness and sinking over the præcordial region. A sensation of want of air is felt, and the respiration is slow and heaving. There is also nausea and even vomiting. The stomach is more affected by compression low down than near the maxilla. When both vagi are compressed fainting and unconsciousness may occur. He tried the compression of both vagi with success in tachycardia, migraine and vomiting.

The vagus may be excited reflexly by deep inspiration, especially by yawning and by deep inspiration followed by forced expiration, the arms being held tightly across the chest in order to increase the respiratory effort.

Bradycardia.—A slow pulse may be congenital, and such cases are better left alone. When it is of occasional occurrence it is generally due to some irritation of the vagus, which may, however, have its action increased by a weak condition of the heart itself. The two indications for treatment are, first, to remove any irritation of the vagus, and secondly, to strengthen the cardiac muscle. The vagus may be stimulated at its roots by increased pressure in the brain, as, for example, in meningitis and in very high tension occurring in chronic Bright's disease, or by the action of drugs such as digitalis, and possibly toxines formed in the intestine. In cases where the tension is high it must be lowered by appropriate treatment, p. 335, and if we suspect toxines we must try to lessen their formation in the stomach and intestines and remove them by free purgation, especially by mercurial salines. If the toxic substances are digitalis and tobacco these must be discontinued, and coffee and tea also if there is any reason to suspect them as causes. Where the slow pulse is due to reflex inhibition from the stomach the gastric mucous membrane should be soothed by the employment of alkalis and bismuth. At the same time bromide of potassium may be employed to lessen nervous irritability. If the attack is very severe the addition of small quantities of opium to the bismuth may be of advantage. Slow pulse from weakness of the cardiac muscle is observed in convalescence from fevers and some febrile disorders, especially diphtheria, influenza, and

chronic myocarditis. In such cases the treatment is to strengthen the heart as far as possible by means of graduated exercises and tonics, especially nux vomica, strychnine, and iron.

Stokes-Adams Disease.—Where this disease is due to lesion of the auriculo-ventricular bundle[10] treatment is of little use, excepting where the lesion is of specific origin. In such cases iodide of potassium should be given in fairly large doses, and, if it is not successful when given alone, mercury should be given along with it, either by the mouth or by inunction. Iodide of potassium may be given up to 60 grs. or more three times a day, *vide* p. 340. In some cases atropine pushed sufficiently far to paralyse the vagus improves the circulation in the whole body and in the heart itself, so that it is not merely a palliative but also more or less a curative remedy. Digitalis, although it tends to produce heart-block, has nevertheless proved useful in certain cases, though whether this is due to stimulant action on the cardiac muscle or not it is at present impossible to say. The tendency to faint may sometimes be averted by sitting down with the head between the knees so as to increase the cerebral circulation, and the inhalation of oxygen appears sometimes to be useful during the attack. Ammonium carbonate has been said to abort the attacks.

Faintness and Fainting.—A condition in which the legs seem unable to support the body and the patient wishes either to sit or lie down. It is often accompanied by chilliness and cold sweat. In severe cases the sight may

become dim and an appearance of a black cloud may shut out all external objects from view. At the same time ringing or buzzing noises in the ears may be felt in the head and yet the patient may retain consciousness. When this condition becomes a little more marked consciousness disappears and the patient will fall to the ground unless supported. These symptoms are caused by insufficient supply of blood to the brain, due to either cardiac failure or dilatation of the vessels, especially those of the abdomen, so that the blood-pressure becomes too low to maintain the cerebral circulation. The symptoms may sometimes be averted mechanically by simply bringing the head down to a lower level so that the blood reaches it, either by making the patient sit with his head between his knees or lying flat on the ground. Relief may be afforded by raising the blood-pressure either by stimulating the heart, contracting the vessels, or both. One of the most common remedies is stimulation of the nasal mucous membrane by carbonate of ammonia (smelling salts)[11] or by strong acetic acid (aromatic vinegar). These substances acting through the nasal branches of the fifth nerve cause reflex excitement of the vaso-motor system, with contraction of the abdominal blood-vessels and consequent rise of blood-pressure. Sponging of the face and ears with cold water or with Eau-de-Cologne has a somewhat similar effect. The heart and vaso-motor system may be stimulated reflexly by means of aromatic spirits of ammonia, brandy, or other strong alcohol, or by hot drinks,

especially hot coffee; sometimes sips of iced water or swallowing pieces of ice may be useful. Warm applications to the hands and stomach, such as hot flannels or hot water bags, help the circulation, and this may also be assisted by vigorous friction over these parts. Fainting may come on in cases of aortic regurgitation, and is then apt to be fatal. In such cases the venous system sometimes, if not always, is greatly engorged, and if the patient is seen at once it is possible that venesection might be very useful. Inhalation of oxygen might also do good if the oxygen were at hand, and artificial respiration might be tried.

Giddiness.—Failure of the circulation to a less degree than that which induces faintness may cause giddiness even in young and healthy persons, but this symptom is very frequently associated in elderly people with some thickening in the semi-circular canals or in the vessels leading to them (labyrinthine vertigo). In such cases giddiness is apt to occur in a very severe form on sudden movement of the head, up or down, or from side to side. In one well-marked case which I had the opportunity of observing, the giddiness only occurred when the head was put backwards and to the left. It could be moved into any other position without the least effect, but as soon as this movement was made intense giddiness came on. In this case the atheroma which probably caused the giddiness extended afterwards to other arteries, and the patient ultimately died of angina pectoris. Where giddiness is due to low blood-pressure

the same remedies are useful as in cases of fainting. In cases of atheroma with high tension, nitrites, iodides, and bromides are all useful, but the liver and bowels should be kept freely acting so as to prevent the accumulation of any toxines. It is sometimes advisable to warn elderly patients who suffer from this symptom to avoid crossing crowded streets alone, as a sudden turn of the head to watch an approaching vehicle might cause such giddiness as to make them fall down in front of it and meet with serious or fatal injury.

Shock.—Operations which will produce shock when anæsthesia is imperfect may be performed without any bad result if the anæsthesia is complete.[12] One great cause of death from shock is that slight but painful operations are performed with imperfect anæsthesia. The previous administration of atropine so as to paralyse the vagus has been recommended as a preventive. When shock has actually occurred the same measures that have already been discussed under the head of fainting are indicated, and at the same time the injection of adrenalin or pituitrin into the veins will have the effect of stimulating the heart and strengthening the vessels. As rapidity of action is very necessary in such cases, the quickest way of giving the remedies is to have them in small capsules containing the dose, which may be at once injected with a hypodermic syringe.

Sleeplessness.—Although insomnia may occur apart from any disease of the heart, it occurs not infrequently along with cardiac disease and

forms one of its most distressing symptoms. The relation between insomnia and the cerebral circulation has already been discussed (p. 200), but it is to be remembered that, apart from the circulation, the brain-cells themselves react with great readiness to stimuli reaching them from any part of the body. Their dendrons are amœboid and have the power of elongation and retraction. In all probability the varied functions of the brain depend on this power, which plays the same part as a telephone exchange. When the dendrons of a cell are elongated so as to meet with those of other cells, communication is established between them and lines of action or trains of thought are established. On the other hand, when the dendrons are retracted the nerve cells become isolated, motor activity ceases as in shock, and mental activity is in abeyance as in sleep.

Stimuli which excite cerebral activity may come from the nerves of special sense of ordinary sensation, or from the viscera. The susceptibility of the cerebrum to such stimuli will depend both on the quantity and quality of the blood it receives, and narcotic poisons circulating through it will lessen or even completely abolish its excitability, while other substances, like the active principles of tea or coffee, may increase its excitability to such an extent that sleep becomes impossible.

When the brain is in an excitable condition, minute stimuli, which under ordinary circumstances would be unfelt, have so much effect

that they will keep a patient awake, and should be carefully looked for and removed.

Powerful or disagreeable impressions on the nerves of special sense must be avoided—no bright light should fall on the eyes—the room should be quiet, and if there is much traffic in a street outside the house its noise should be deadened by laying down straw or tan. At the same time soft monotonous sounds, such as reading aloud, are powerfully soporific. There should be no disagreeable smell in the room, and commodes should be at once emptied after being used. Even flowers, although they make the sick-room brighter in the day, should be removed at night. A persistent bad taste in the mouth may be best removed, as a rule, by washing the mouth out with a lotion of hydrogen peroxide. The pain of aching teeth may be lessened by washing out the mouth with a solution of sodium bicarbonate, which neutralises those acids in the mouth which irritate exposed nerves. Instead of this a mixture of sodium bicarbonate and laudanum may be rubbed over the gums and between the teeth and applied on a pledget of cotton-wool to any carious cavity.

Cold feet are a common cause of sleeplessness, and the condition may be relieved by wrapping them in dry warm flannel and placing an india-rubber bag filled with hot water and covered with flannel close to them. Such a bag is better than the stone bottles often used, as it can be more thoroughly applied to the feet, abdomen, nape of neck, or any other part of the body that may be cold. Great care should be taken,

however, that both bags and bottles should be carefully enveloped in flannel, for I have seen bad burns caused by the want of this precaution. Sometimes instead of putting the feet into hot water or applying hot bags to them it is better to put the feet, one at a time, into cold water, rub them with some rough substance, such as a loofah, and then dry them with a warm towel. When the feet are put into hot water the vessels of the skin become dilated at the time, the feet are red and warm, but its effect soon passes off, the vessels of the skin again contract and the feet again become pale and cold. The dilatation of vessels caused by rubbing and cold water is more permanent than that caused by putting them in hot water.

Sometimes instead of being too cold the patient is prevented from sleeping by being too hot. If the bedroom is not too cold to allow of its being done with safety, the removal of all the bedclothes, with perhaps the exception of a single sheet, for ten minutes or quarter of an hour will allow this feeling to pass off and the patient to get to sleep. If he is strong enough, to walk a short time round the room in his night-shirt while the bed is aired and cooled it is even better. Sometimes patients complain of the weight of the bedclothes, and in such cases the substitution of an eider-down quilt for blankets may be a comfort. For patients who are well enough to take it, a warm bath sometimes helps much to bring on sleep, and its quieting influence is even more apparent in children than in adults. It should be warm, but

not hot, because too high a temperature tends to excite the heart, to produce palpitation (p. 415), and to prevent instead of inducing sleep. The warm water tends to dilate the vessels of the skin, and by drawing away blood into the cutaneous, to lessen the amount in the cerebral area (p. 20). But its chief action appears to be that of softening the skin, removing sweat, and soothing the cutaneous nerves. Instead of a warm bath, sponging over the body and limbs may be employed either at the usual time of going to sleep or during the night if the patient is very sleepless. Even sponging of the face, hands, and feet with warm water is often sufficient. If the patient is feverish it is a good plan to sponge the whole surface of the body with warm water, which should not be completely dried off but simply dabbed with a soft napkin, so as to leave the skin somewhat moist, as if the patient had been perspiring gently. The patient's night clothes are not again put on, but the whole body should be covered by one long cradle or two short ones placed end to end. Over this is thrown a single sheet or blanket so that the moisture from the patient's skin evaporates and cools the body, the cooling process being more complete because the warm water tends to dilate the cutaneous vessels, and by thus bringing the blood to the surface aids the cooling process. When the patient is very feverish it is sometimes advisable to leave the end of the cradle open so as to allow a freer circulation of air under it. One fact which seems to show, however, that the soothing

effect of sponging is chiefly due to its soothing effect on the cutaneous nerves rather than to any action on circulation or temperature is that very gentle massage has a similar effect. It should consist in exceedingly gentle stroking movements over the back, limbs, and heart, and any strong rubbing is generally useless or harmful except when the patient has "the fidgets," when gentle kneading of some muscles, and especially of the calves of the legs, may be useful. Stroking the head and brushing the hair with a soft brush are sometimes helpful. Children seem naturally to massage their eyeballs when they are sleepy by doubling their fists and rubbing their eyeballs with their knuckles, and very gentle rubbing over the closed eyelids in a circular direction with the tip of a finger if well done has a singularly soothing effect. Any local source of irritation should be soothed, such as bed-sores, patches of eczema, or pruritus and piles.[13] Pruritus ani is a potent cause of sleeplessness.

If the rectum is loaded the itching is usually worse, so an enema of warm water is advisable in such cases, followed by the introduction of a suppository of hamamelis alone or with conium, cocaine, or bismuth.

The itching may sometimes be quickly allayed by applying to the anus a sponge dipped in water as hot as can be borne. Instead of plain water strong solutions of sodium or potassium carbonate or bicarbonate may be used. Other useful lotions are solutions of boric acid 4 per cent., of phenol 2 or 3 per cent., of liquor carbonis or liquor picis carbonis, 1 to 5 per cent. If the

itching is severe these lotions may be made even stronger, but if too strong they cause pain. Their efficacy may be increased by the addition of 2 per cent. of cocaine. After washing, calomel dusted on or calomel ointment is useful. Other useful ointments are those of conium, cocaine, carbolic acid, resinol, boric acid, methyl salicylate and menthol, calomel, bismuth, subacetate of lead, and hamamelis.

When other remedies fail it may sometimes be relieved by painting tincture of iodine around the anus, and the pain this causes may be lessened by applying a solution of cocaine before and cocaine ointment afterwards.

Obstinate cases are sometimes cured by X-rays.

If flatulence or acidity persist in spite of treatment it may be advisable to put the patient on a pure milk diet for several days.

Milk alone is apt to become very disagreeable, but if it is flavoured with a little tea, coffee, or cocoa, it can be taken much more readily. The sour milk recommended by Metchnikoff is very useful in lessening flatulence and indigestion. Milk contains a large quantity of lime and therefore tends to act as an astringent. It is apt also to form large clots in the stomach unless it is previously peptonised; these clots are very indigestible; they may pass down the bowel and cause very large and very hard motions. This is especially the case if the milk is taken in very large draughts, and in some Continental milk cures the patient is advised between every mouthful of milk to chew carefully a very small piece of

dry hard biscuit. The constipating effect is lessened by peptonising, and if the milk is over-peptonised it may sometimes even cause diarrhœa. The formation of hard constipated motions may be partly prevented also by the administration of half an ounce of liquid paraffin every night at bedtime.

The stomach and bowels require careful attention. Overloading of the stomach by a heavy meal, of the bowels by constipation, or distension of either by flatulence is apt to interfere with sleep. It is advisable that no large meal be taken within three or four hours of bedtime; fæcal accumulations should be removed from the bowels by enemata or laxatives (p. 375), and flatulence by carminatives (p. 360). A very acid condition of the gastric contents tends to prevent sleep and should be counteracted by alkalis (p. 356). While too full a stomach is opposed to sleep, a very empty condition has a similar action, and warm, light, digestible food in not too great quantity tends to induce sleep. The warmth tends to dilate the vessels of the stomach and thus deplete the cerebral area (p. 20), but if the food is too hot the heat is transmitted through the diaphragm to the heart, quickening its beats and, by thus accelerating the circulation, stimulating instead of soothing the brain. Peptonised milk or some of the numerous patent foods may be given at bedtime, and some may also be kept in a "thermos" flask or baby's food-warmer and given at intervals during the night if the patient is wakeful.

A warm poultice over the abdomen or an abdominal compress tends to dilate the abdominal vessels. The compress may be made either with hot water or with cold. It is easily prepared by wringing a towel out of hot or cold water, folding it to the proper size, covering it with oiled silk, putting over this a sheet of cotton wool or Gamgee tissue and fastening it in place with a many tail bandage. A wet pack over the whole body has a somewhat similar action, but I think in this the arms ought not to be included, because the feeling of restraint is very disagreeable and may lead to struggles which will be very injurious. This, I believe, is the cause why sudden death has sometimes occurred from the application of the wet pack.

Sometimes the sleeplessness may be due to lack of tone in the carotids, so that the moment the patient lies down the blood pours in full stream through the brain and sleep becomes impossible. In some of those cases the same lack of tone occurs in other vessels of the body and the patient is drowsy whenever he sits up. For this condition the best remedy, probably, is digitalis in 5 or 10 minim doses, combined with bromide of sodium, potassium or ammonium in 20 or 30 gr. doses. I have seen a case in which persistent sleeplessness seemed to be due to atheroma of the carotid arteries, which felt as hard as pipe stems under the fingers. After a course of iodide of potassium and gentle massage over the arteries this hardness became very much less and sleep was obtained.

Hypnotics.—Hypnotics may be divided into (1) those that act upon the circulation, (2) those that act upon the brain cells, and (3) those that act upon both. Amongst those that act upon the circulation I think digitalis comes first and foremost, from its steadying effect upon the heart and its power to give tone to the vessels. Strychnine also probably acts in a similar way. Some years ago I described a case of persistent sleeplessness due to continuous hard mental work and where ordinary hypnotics were inadvisable.[14] A full dose of nux vomica at bedtime brought up the patient's condition from that of being over-tired, when sleep is generally poor or absent altogether, to that of being simply tired, where sleep is sound and refreshing. All the alcohols tend to dilate vessels, to lessen blood-pressure, and ultimately to diminish the activity of the nervous tissues, although at first they may seem to have a stimulant action. For this reason half an ounce to an ounce of old whisky or brandy in two or four ounces of hot water at night is even more efficient as an hypnotic than the warm milk already spoken of. But in place of adding the spirit to water it may be added to the warm milk, and this combination is a very useful one. Of the other substances belonging to the alcohol series the most useful is paraldehyde,[15] which in doses of half a drachm to a drachm often induces refreshing sleep and is probably more free from any danger than almost any other hypnotic. It is best given with a little alcohol and water at night. Its great drawback is its

disagreeable and pungent odour, which remains in the patient's breath for very many hours after it has been taken.

Chloral tends to a certain extent to depress the action of the heart, and for this reason one is inclined to be careful in giving it to patients with a weak heart. On the other hand, in patients with high tension and a powerful heart this effect of chloral upon the circulation aids its action as a hypnotic.

Although Oscar Liebreich[16] renounced the idea which led him to use chloral as a hypnotic, viz., that in the alkaline blood it would break up and yield chloroform which would then act on the nervous system, yet he still remained convinced that if chloral is used for any length of time the patient ought to have an alkaline course also.

The fatal effect of an overdose of chloral, such as may sometimes occur from an idiosyncrasy on the part of a patient, is to a great extent due to dilatation of the peripheral vessels and consequent loss of heat from the body. It may sometimes be averted by the simple application of warm water bags or heated flannels to the body.[17]

Butyl chloral is of little use as a hypnotic. Chloral is decomposed by alkalis into formic acid and chloroform and so cannot be mixed with ammonia, but a compound of chloral and ammonia, called chloralamid, has been introduced with the idea that the ammonia would counteract the depressing effect of the chloral on the heart. In doses of 15 to 45 grs. (1 to 3

grs.) it is sometimes useful. Like chloral, it is decomposed by alkalis.

Chloralose is a compound of chloral and glucose. The usual dose is 3 to 10 grs. Opinions are divided as to its safety and depressing action on the heart.[18]

Many mixtures of chloral and other hypnotics have been introduced[19] under various names, but if it is desired to prescribe mixtures it is better to do so for definite quantities of each drug adapted to each patient than under the name of a drug of which the composition may be unknown or forgotten.

Another group of hypnotics, in which sulphur instead of chlorine is combined with an alkyl radical, contains sulphonal, trional, and tetronal. The dose of the first two is 10 to 30, that of tetronal, which is the most toxic, is 10 to 20 grains. Sulphonal[20] is the most widely used of the three, but it is sparingly soluble, and is best given with hot brandy and water. It is slowly excreted, and if repeated too frequently, cumulative symptoms may result.

Another group of hypnotics consists of substituted ureas. Urethane[21] (ethyl carbamate) is mild and safe in doses of 10 to 60 grs. Hedonal[22] is nearly allied to urethane, but while it is also safe it is unpleasant to take and may produce disagreeable symptoms. Veronal[23] was a very favourite hypnotic in doses of 2 to 10 grs., but fatal poisoning has occurred even with this apparently small dose. Medinal is the sodium salt of veronal, and being a more soluble salt, is more rapid in its action. Adalin[24] in doses

of 5 to 10 grs. three times a day is a useful sedative; in doses of 10 to 15 grs., followed by a hot drink half an hour before bedtime, it is said to be a prompt hypnotic, and suitable for cases of heart disease.

In many cases of heart disease a very distressing form of sleeplessness occurs. The patient is intensely drowsy, but the moment he falls asleep he has feelings of intense distress and wakes with a start. Various hypnotics may be tried, but the remedy *par excellence* in this condition, however, is opium or morphine. The latter may be given either by the mouth or subcutaneous injection, and the former either by the mouth or rectum. A convenient way is to draw 30-60 minims of tincture of opium into a glycerine syringe holding 2 drachms, then draw up water till the syringe is full, and inject into the rectum.

The advantage this method has over administration by the mouth is that one can be quite sure beforehand that the rectum is empty and that absorption will take place quickly, whereas the stomach may contain a large quantity of food or fluid with which the opium will be so much diluted that it may have hardly any effect. Sometimes neither opium nor morphine seem to produce the desired effect, even when given in full doses, and in such cases a few whiffs of chloroform may be given so as just to allow the narcotic to take effect.

And here it may be well to say that I do not think the presence of albumen in the urine contra-indicates the use of either

opium or morphine. The susceptibility of patients to these drugs varies so much that it is impossible to fix a dose, but usually one may begin with $\frac{1}{6}$ or $\frac{1}{4}$ of a grain of morphine subcutaneously, and increase the dose carefully until the desired result has been obtained. Even should there seem to be danger in pushing the narcotic, it must be remembered that to withhold it also entails risk, for the exhaustion of the patient by continued insomnia cannot but tend towards a fatal termination.

Intermittent and Irregular Pulse.—In cases where intermittence and irregularity depend upon mechanical changes outside the heart from adherent pericardium[25] the most efficient plan of treatment is probably to strengthen the heart, so as to enable it to overcome the additional resistance by tonics and graduated exercises. Although one would not recommend it, it would appear that occasional severe exercise has had the effect of restoring the cardiac condition to the normal. In cases of definite heart-block there is little chance of removing it unless it is of syphilitic origin, in which case mercurials and iodides might be useful.

The same results as those from imperfect heart-block may occur even from weakening of the impulses sent down by the auricular ventricular node. I think I have seen this result occur temporarily in consequence of the administration of an overdose of mixed antipyrin, phenacetin, and aspirin to relieve neuralgia. Such weakness is a cause of intermittent pulse. The treatment is, of

course, to strengthen the heart by strychnine, caffeine, and digitalin, or strophanthus, and probably camphor might also be useful. In cases where the heart is organically diseased, as in mitral stenosis or regurgitation, these conditions must be treated according to the gravity of the condition (*vide* p. 402). In the great majority of cases, however, even if organic disease be present, the intermittence or irregularity of the heart depends upon some reflex stimulation of the cardiac nerves, and especially of the vagus. It has already been mentioned, at page 73, that this nerve may be stimulated reflexly from almost any organ in the body, and one of the most frequent sources of such stimulation is dilatation of the stomach or intestines by wind or the presence in them of irritating substances. Very frequently indeed the administration of carminatives so as to bring away flatulence will quickly remove the intermittence or irregularity. This action is much assisted by the simultaneous administration of bromides to lessen reflex action. If there be much irritation of the stomach, an emetic of plain hot water or hot water and mustard may give relief by removing the irritant. Other carminatives may be used (p. 360) to bring the flatulence away, and I give here two prescriptions, which may serve as examples :—

℞ Sodii Bicarb.	gr. v
Spt. Æther Co.	♏ v
Spt. Chlorof.	♏ v
Tinct. Cardamom. Co. . . .	♏ x
Aq. Menth. Pip. . . .	ad ℥j

M. mitte ℥viij

Sig. One-eighth part to be taken alone, or with water, every ten or fifteen minutes until the flatulence is relieved.

℞	Spt. Ammon. Aromat. . . .	♏xv
	Spt. Chlorof.	♏x
	Tinct. Carminativ. . . .	♏x
	Aquam	ad ℥ss

M. mitte ℥vj

Sig. One-twelfth part to be taken alone, or in water, every few minutes until the flatulence is relieved.

Another useful plan is to give about one-third of a teaspoonful of sodium bicarbonate in a claret glassful of water or peppermint water, and to let the patient slowly sip as much of this as is necessary. But, in order to relieve the palpitation permanently, the digestion must be put right and fermentation in the stomach stopped. We must remember here that the blood from the stomach has to pass through the liver before it reaches the general circulation, and that the liver and bowels require attention as well as the stomach. We very frequently are able to relieve palpitation far more by medicines which act only on the digestive canal, than by drugs which affect the heart and vessels directly. One of the best remedies that I know for functional irritation of the heart is one which my old teacher, Dr Warburton Begbie, used to call the "pulvis mirabilis." Its composition was as follows:—

℞	Bismuth Subnit. . . .	gr. x
	Sodii Bicarb.	gr. x
	Pulv. Nuc. Vom. . . .	gr. ss-jss
	Pulv. Rhei.	gr. j-iij
	Pulv. Cinnamom. Co. . . .	gr. iij

M. ft. pulv. To be taken before each meal.

The great disadvantage of this powder was its filthy taste, but this can be got over by putting the nux vomica and rhubarb in a cachet, and giving the other ingredients in a mixture, along with some carminative and flavouring substance. Both the mixture and cachet are taken at the same time, and, as they mix in the stomach, one gets the effect one desires without the patient perceiving the taste. When the heart is feeble, 3 or 4 minims of tincture of strophanthus or of digitalis may be added to the mixture with advantage; and if the patient be anæmic, some preparation of iron may be either given along with or separate from the medicine.

Cardiac Pain.—I have already mentioned that pain in the cardiac region may sometimes be due to leucorrhœa. Whether this is caused by reflex action or by general depression I am unable to say, but it usually yields readily to iron, the preparation which I have commonly used being 15 minims of solution of perchloride of iron in an ounce of infusion of quassia three times a day. I have seen pain in the cardiac region persist in a patient for years. It was probably connected in some way with cardiac innervation, for the patient's pressure was very low and the pulsation was sometimes intermittent. It was very markedly increased before or during change of weather, and in such cases an anti-rheumatic treatment by salicylates combined with tonics is probably best. I have also seen pain in the cardiac region lasting for many months which was probably due to some form

of intercostal neuralgia. The patient had formerly had an attack of shingles, but there were no vesicles to be found on the place where this neuralgic pain was felt. In such cases local treatment by the use of some sedative ointment over the seat of irritation should be tried, and in a case associated with shingles I have found blisters and a cautery over the roots of the second, third, and fourth dorsal nerves of the affected side give a certain amount of relief. Electrical treatment should also be applied either by the static current or by ionic medication.

Treatment of an Attack of Angina Pectoris.—The indication for treatment, of course, is to relieve the heart by dilating the vessels, coronary[26] (*cf.* p. 191) as well as systemic, and this is brought about most quickly by the use of nitrite of amyl.[27] Nitrobutyl and other organic nitrites[28] have a similar action, but nitrite of amyl seems, upon the whole, to be the most satisfactory. Nitroglycerine[29] acts nearly, though not quite as quickly, and is more convenient. It has also the advantage of dilating the vessels for a longer time than nitrite of amyl. It may be given in solution with a little brandy or ether, or the patient may carry about with him nitroglycerine tablets, each containing one-hundredth of a grain, made up with chocolate; and the best plan, as a rule, is not to swallow the whole tablet, but to nibble it slowly until the pain has ceased. If half a tablet is sufficient, it is not necessary to take more; but if one is insufficient, then as many more may be taken as

are necessary. I have never seen any bad effect from an overdose either of nitroglycerine or amyl nitrite, except headache, giddiness, or transient faintness. During an attack of angina the pain frequently becomes relieved by the spontaneous expulsion of wind from the stomach, and a mixture of nitroglycerine with carminatives such as the following is sometimes very useful:—

℞ Liquor Trinit.	.	♏j
Spt. Ammon. Aromat.	.	♏xv
Spt. Aether. Co.	.	♏x
Spt. Chloroform	.	♏x
Aq. Menth. Pip.	.	ad ℥j
M. mitte ℥viij		

Sig. One eighth part every five or ten minutes till relief is obtained.

When the attack is excessively severe a neuralgic element may be superadded to the physical condition, and I think it is possible that sometimes it may come on independently. At any rate, a subcutaneous injection of a quarter or a third of a grain of morphine may sometimes be necessary, in order to lessen the pain and give the patient relief, and a few whiffs of chloroform will deaden the pain until the morphine has had time to take effect.

If necessary, the morphine must be pushed until the pain is relieved. The risk from the attack is much greater than that from an overdose of morphine. A dose may be required which, under ordinary circumstances, might be regarded as extremely dangerous, but unless the morphine is given in sufficient quantity it is useless.

Diet and Regimen in Angina.—During the interval the tension should be kept low by diet, as nearly as possible vegetarian, taking care that it is easily digested and that it does not give rise to flatulence. Tea and coffee, and, of course, all meat extracts which contain substances of the purin type and tend to raise the blood-pressure, should be avoided. The bowels should be kept freely open, and mercurials should be given, once, twice, or three times a week at night, followed by a saline in the morning, so as to remove from the body all substances likely to raise the blood-pressure. Many substances having a poisonous action are absorbed by the liver and excreted in the bile. They are reabsorbed from the duodenum, again passed to the liver, and again excreted. This may go on for a long time in the enterohepatic circulation, until they either accumulate to such an extent that they pass into the general circulation and act upon the nervous system, heart, or other organs, or are cleared out by mercurial purgatives and salines (p. 354). Nitro-erythrol,[30] in doses of half a grain three times a day, or more if required, will sometimes keep a patient, who would otherwise suffer from angina pectoris, perfectly comfortable for years. The hippurates of sodium and ammonium recommended by Oliver,[36] in doses of 5 to 30 grs. three times a day, are useful in some cases in lowering the tension. Iodide of potassium, in doses of 5 to 30 grs. three times a day, is good if the patients can stand it. It is remarkable that patients who cannot stand the smaller

doses can take 10 grs. or more with comfort. If iodide of sodium, of potassium, or of ammonium cannot be borne, the organic compounds of iodide such as iodoprotein, iodoglidine, sajodin, tiodine, iothion, or iohydrin may be tried. Guipsine, a preparation of mistletoe, has been found useful by some observers (p. 340). The usual dose is 6 to 10 pilules, or one to two intramuscular injections daily. Perhaps its failure in some hands may have been due to too small a dose. Electrical treatment may also do good (*cf.* High Tension, p. 454).

All such persons, however, should take care to remain quiet for half an hour at least after every meal, and when they get up they should move very slowly until they begin to get warm. When the vessels of the muscles become dilated, patients are frequently able to walk with perfect comfort even at a rapid pace. *Cf.* Influence of muscular area, p. 18.

Angina Abdominis.—An attack of angina abdominis[31] is to be treated like one of angina pectoris, but during the intervals not only should the digestion and bowels be carefully regulated, but antipyrin in 10 gr. doses may be tried two or three times a day, because of its effect upon the spinal cord, which is so well-known in the relief of tabes.

Cardiac Asthma.—When the right side of the heart is enfeebled the symptoms of cardiac asthma are apt to come on. The patient is quite comfortable so long as he remains still, but the least exertion brings on rapid breathing,

or even dyspnœa and distress. This condition is largely due to degeneration of the right side of the heart, consequent upon interference with the circulation in the right coronary artery. It may be associated with fatty degeneration of both sides of the heart, but it may also occur in the right side independently of the left.[32] Nitrite of amyl is not of so much use in this as in ordinary angina, as the pulmonary circulation does not seem to be affected by nitrites to the same extent as the general circulation. Inhalation of 5 minims of iodide of ethyl is sometimes serviceable, but inhalation of oxygen occasionally affords very great relief, and in a case which I recently saw the tension in the radial artery rose under the influence of oxygen to an extent which I should not have believed if I had not seen it. The tension, as tested by Potain's instrument, was only 75 when the inhalation was begun, and in the course of ten minutes' inhalation it rose steadily until it had reached 150. Hypodermic injections of morphine may be required, as for angina pectoris. The iodide of ethyl or nitrite of amyl may be given along with oxygen (Fig. 77, p. 242).

In cardiac asthma gentle exercises are useful as tending to train the heart, increase its nutrition, and thus accelerate the circulation through the lungs. At the same time, iodide of potassium, strychnine, digitalis, squill, and strophanthus are all useful, as well as Oertel's treatment (p. 250).

On the Treatment of Headache.—Headache is a general term which comprises many differ-

ent conditions. The part of the head affected differs very greatly, so that commonly one has to the term added some word to express its position, such as frontal, temporal, vertical, or occipital. The kind of pain also varies very greatly. Sometimes it is a dull, heavy, aching pain, which seems to pervade the whole head and renders thought almost impossible, while at other times the pain may be of an intense stabbing or boring character, excessively severe, limited to one part of the head or one temple, and yet the brain may be perfectly clear, and indeed the mental faculties may be even more acute than usual. The pathology of all these kinds of headache have not been made out to any degree of certainty. I have already described, at p. 184, what I believe to be the pathology of migraine, and some other forms of headache may be also dependent upon vascular congestion in one place and vascular contraction in another. Whatever be the immediate cause of the pain, it seems highly probable that it is due in many cases to toxæmia, the action of the toxins being directed to the head by some local source of irritation. When either the toxæmia or the local irritation is relieved the pain may cease, although the other factor in the causation of the headache remains unaffected. Amongst the most common determining local causes are eye-strain, due to inequality of the focal length of the eyes, astigmatism, or weakness of convergence.

The teeth are a common cause of headache, and irritation in them may arise either from

decay with exposure of the pulp in a cavity, or inflammation of the gums, pyorrhœa, or irritation of the gums or of the teeth by acid secretion in the mouth. The nose is a frequent cause of persistent headache, especially of vertical headache, and attention must be paid to post-nasal catarrh and to the possibility of inflammation of the antra or sinuses. The ear should not be forgotten, especially if there is any discharge or if there is deafness, but it is less common than the other causes. Headaches depending upon the eyes are sometimes cured by the use of proper glasses, those depending upon the teeth by extraction of the decayed tooth, or by washing the mouth with a solution of bicarbonate of soda, or rubbing a mixture of bicarbonate of soda and laudanum over the gums and applying it on a pledget of cotton wool either on or between the teeth. Irritation in the nose may be treated by nasal douches and sprays, but if the irritation persists it may be necessary to consult a specialist upon the subject. But the double origin, local and general, of headaches is shown by the fact that sometimes even while local sources of irritation already mentioned remain unaltered, the headache may be relieved on the removal of toxins from the body by means of a mercurial pill and saline purgative. Patients who suffer from continuous high tension are apt to have attacks of headache, sometimes extremely severe. The curious fact about these attacks is that sometimes the patient seems to have no recollection of the attack, although during it the pain

appeared to be excruciating. In such cases lowering the tension by mercurials, salines, iodides, nitrites, etc., tend to keep the headache away. During the attack the feet sometimes become very cold, and a hot foot-bath or hot applications to the feet tend to relieve it. An india-rubber bag filled with hot water placed under the nape of the neck is sometimes still more efficacious. Cold lotions to the forehead are grateful to the patient, as they usually lessen the acuteness of the pain. When the headache lasts several days in succession, blisters, the size of a shilling, to the temples or nape of the neck sometimes give relief. Drugs containing a carbon ring-nucleus are usually more useful than others. They are salicylate of soda, phenacetin, antipyrin, antikamnia, aspirin, pyramidol, migrainine, etc. What suits one patient does not always suit another, nor are these drugs always equally efficacious in the same patient at different times. Perhaps those most generally useful are phenacetin and antipyrin, in doses of 8 or 10 grs., either alone or combined with about 2 grs. of caffeine. If the headache is fully established little or no absorption may occur from the stomach, and medicines taken at these times will have no effect whatever. But even when the headache is extremely severe and accompanied by constant vomiting, 10 grs. of antipyrin with 2 grs. of caffeine may be dissolved in 2 or 3 fluid drachms of water and injected into the rectum. Absorption from the bowel does not seem to cease at the same time as

absorption from the stomach, and relief may be afforded in this way. The pathology of the headache which with many people comes on with the menstrual period, whether they are otherwise healthy or suffer from cardiac disease, is uncertain, but it is probably connected in great measure with alterations in the cranial circulation, and probably alterations in the pressure within the cranial vessels. One of the most important remedies for this, of course, is rest, and relief can be afforded to a certain extent by the other medicines which I have already mentioned. Massage may also relieve.

Where patients are liable to awake in the morning with a slight headache, which gets worse and worse during the day, its occurrence may frequently be prevented by taking at bed-time on the previous night 10 to 20 grs. of sodium salicylate (natural) with 15 to 30 grs. of potassium bromide and half to one drachm of aromatic spirit of ammonia.

Many such sufferers know when to expect a headache, either because it usually follows some unusual exertion, excitement, or eye-strain, or because they have beforehand a warning in the shape of either unusual well-being, depression, or irritability.[33]

Flushes of Heat and Morbid Blushing.—Both of these symptoms, though not dangerous, are very annoying. The most useful remedies in them are valerian, sumbul, and the bromides. Valerianate of zinc, compound asafœtida pill, 2 grs. of each, have been recommended to be taken night and morning. When they occur

at the menopause 15 minims of the tincture of perchloride of iron, taken three times a day, is sometimes useful, and tabloids of ovarian extract may also be tried.

Raynaud's Disease.—It has seemed to me that this disease is frequently associated with a rheumatic tendency, and I have used with advantage the natural salicylate of soda and bromide, 10 grs. of the former and 15 of the latter, three times a day if the patient is below par. Strychnine and arsenic may be given, 5 minims of the solution of it immediately after meals twice or three times a day. As cold brings the attack on, the part should be kept as warm as possible, and woollen gloves and socks may be worn at night. The feet may be previously rubbed with an ointment of salicylate of methyl. Small doses of thyroid may be given, beginning with half a grain every night and increasing it up to as much as 5 grs.

Chilblains.—In this condition I have also found small doses of thyroid useful. Lactate of calcium,[34] 5 grs., in the form of a tabloid, three times a day, has been recommended, and in elderly people a combination of nitro-glycerine and strophanthus. If the chilblains are broken boric acid ointment is one of the best applications. Urticaria sometimes comes on acutely from some indiscretion in diet and in consequence of taking shellfish, especially mussels. This may be relieved by an emetic or by purgatives.

Chronic Urticaria. — This is a most persistent and troublesome ailment. Intestinal antiseptics (p. 359) should be used, and ichthyol,

in doses of 5 grs. in capsule three times a day, has been specially recommended. Magnesia, either calcined or the carbonate, in 20 gr. doses three times a day, occasionally relieves it; and if this is not sufficient to keep the bowels freely open, magnesium sulphate may be given in addition. The itching may be allayed by the remedies already recommended for this (p. 429). If any source of microbic infection can be obtained a vaccine should be made from it and the patient treated with it.

Low Tension.—One of the commonest causes of this is over-smoking (p. 328), and when the tobacco is stopped the tension gradually rises. As I have already mentioned (p. 181), when low tension is persistent one must examine the lungs carefully for any trace of tuberculosis. In a number of cases it is associated with neurasthenia, and the treatment must then be directed to improve the digestion so as to increase the assimilation of food, to strengthen the appetite generally by the use of tonics and graduated exercises, and the avoidance of over-work, and especially of worry, as far as this is possible.

High Arterial Tension.—High arterial tension in itself is not an entirely bad thing to be got rid of at all costs. In this respect it resembles pain, fever, inflammation, and suppuration. Pain is nature's warning that something is going wrong and ought to be put right; fever is one of nature's defences by which microbes which have invaded the body may be destroyed. Inflammation, with its accompanying accelerated circulation, is intended for the repair of damaged

tissues; while suppuration is the indication of a conflict between defensive phagocytes and invading microbes. But pain may become so intense as to be unbearable and to render death preferable to life. The temperature in fever may rise so high as either to destroy life at once, or seriously damage the vital organs. Inflammation may go on to destruction instead of repair of the tissues, and suppuration may lead to accumulations of pus which require surgical interference for their removal. In the same way high tension and the cardiac hypertrophy which usually accompanies and helps to maintain it, are a provision of nature in order to maintain the circulation in spite of increased resistance, so that it is beneficial to the organism, and many men who have it are distinguished by their extraordinary vitality, energy, and power of work and endurance, both physical and mental, the high tension keeping up an abundant supply of blood to all the organs. But, nevertheless, high tension is a source of danger, and it may cause death either through cardiac failure or, more commonly, rupture of a vessel in the brain.

Treatment of Senile Conditions of the Vessels.—Although I do not quite agree with him in every respect, I think that my former pupil and old friend, Dr Haig,[35] has done a very great service by drawing general attention to the injurious effects of a too highly nitrogenous diet. In cases where the arterial tension tends to rise much above the normal, the proteins in food should be kept as low as they possibly

can, consistently with the proper performance of the bodily functions. The bowels should also be kept free, either by the use of salines or by small quantities of some aperient such as cascara, aloes, or rhubarb, along with each meal, so that the natural stimulating effect of food upon the bowels as well as the stomach may be increased. Nor should the occasional use of a mercurial purgative be omitted; and here I may mention that the danger of mercury in albuminuria has, I think, been greatly exaggerated, and has sometimes in my own experience been productive of much harm, for I have met practitioners who have been so imbued with the fear of mercury that they would not give it in cases of cardiac disease either as a purgative or in combination with digitalis, because albumen had appeared in the urine; whereas in these very cases mercury was one of the best things to restore the circulation to its normal condition and cause the albumen to disappear.

The steady employment of iodides is sometimes most useful, and I have found great advantage in a number of cases of high tension from 20 grs. of nitrate of potash along with $\frac{1}{2}$ to 2 grs. of nitrite of sodium given in a tumbler of water or aperient water *every morning* on rising. This seems to keep the tension from rising too high, and the treatment may be continued with advantage for years.

Where this is insufficient, it may be supplemented by 2 or 3 grs. of sodium nitrite in water every four hours, or by nitro-erythrol

in doses of $\frac{1}{2}$ to 2 grs., or $\frac{1}{100}$ gr. nitroglycerine in tablets or solution. Ammonium hippurate, as recommended by Oliver,[36] may also be useful. Electrical treatment by high frequency currents as a rule is successful in lowering the tension, at least for a time.

In very high tension it may be advisable to bleed from the arm. The effect of this in relieving angina was most strikingly shown in the patient whom I was afterwards able to relieve by the use of nitrite of amyl.[37]

By careful estimation of the blood-pressure, and by keeping the tension at a proper level by diet regimen and medicines, I believe that the cardiac failure or the cerebral apoplexy, which are common causes of death in advanced years, may be averted for years, and the life not only prolonged greatly, but the senile decay or paralysis, which are so trying to the patients themselves and their friends, may be prevented.[38]

Aneurism.—The indications in aneurism are: first, to lessen pressure, so as to prevent further distension; second, to keep up the general nutrition, so that the diseased artery may be nourished as well as the rest of the body, and thus prevent it from yielding further; third, to induce cure by means of clotting inside the vessel if possible; and fourth, to relieve pain. Avoidance of any strain, mental or bodily, and the measures calculated to lessen pressure are to be adopted (p. 335). A certain amount of exercise without strain is, I think, advantageous by keeping the body generally in a good condition, and if this cannot be had, its place may

be taken to a certain extent by massage. Clotting may be favoured by a considerable amount of milk in the diet and the administration of lime salts such as calcium chloride,[39] 10 gr. doses or more three times a day. The most efficacious remedy for relieving pain is, I think, usually iodide of potassium, but it must be given in large doses. Anything under 20 grs. three times a day is, I think, generally useless, and to be efficient it must generally be given in doses of 30 grs. three times or more a day.

Cerebral Hæmorrhage.—When a vessel has ruptured in the brain one of the first objects in treatment is to lessen the blood-pressure, so as to prevent, as far as possible, further hæmorrhage from taking place. Probably the quickest way of doing this is by bleeding from the arm, an old-fashioned remedy too much neglected. It not infrequently happens, if the hæmorrhage is severe, that the blood becomes venous and will not flow when the vein is opened. If this is the case, oxygen should be used if possible (p. 147). The patient should be kept perfectly quiet, in the recumbent position but turned slightly on one side, with the head somewhat raised, so as to lessen the pressure in the cerebral vessels. Hot water bags or bottles may be applied to the feet and hands, and mustard leaves to the calves of the legs, so as to draw the blood from the brain as far as possible, but care must be taken not to burn the skin. The bowels should be opened by 5 grs. of calomel or half a minim to a minim of

croton oil mixed with 30 minims of either castor, almond, or olive oil, and placed on the tongue. Should the patient gradually recover, the diet should be chiefly or almost entirely milk for several days, but if the coma should be of long duration nutrient enemata may be employed. After recovery the dietetic and medical treatment should be that for high pressure. If the patient after recovering consciousness has much headache, leeches should be applied over the temples or behind the ear, or small blisters about the size of a shilling over the same places.

Cerebral Thrombosis.—The condition here is usually exactly the opposite of that in hæmorrhage, the blood-pressure being low and the blood poor, so that clotting occurs readily. In treating it, however, complete rest is required also, but instead of remedies calculated to lower the blood-pressure, stimulants to keep up the circulation are necessary. The best of these probably is strychnine, in doses of $\frac{1}{60}$ to $\frac{1}{30}$ of a grain given hypodermically. In order to lessen the tendency to clot, citric acid or citrate of potash may be given, either in the form of citric acid itself in 15 gr. doses or the juice of half a lemon, sweetened if required. Theoretically, at least, milk is objectionable; it contains a large quantity of calcium salts, and therefore tends to increase the clotting power of the blood and to constipate the bowels. It is desirable that the bowels should be kept open, but only by gentle purgatives, and not by such drastic purgatives as in cerebral hæmorrhage. Beef

tea and strong soups are indicated, while in cerebral hæmorrhage they would be objectionable. In cases where there is any suspicion of the thrombosis depending upon syphilitic endarteritis, iodide of potassium should be administered, and if necessary mercurial inunction may be employed. Even in cases where there is no suspicion of a specific disease iodide of potassium may be given in the hope of causing absorption of the thrombus.

LITERATURE.

1 Lauder Brunton, "On Digitalis," Prize Thesis (London : Churchill); reprinted in *Collected Papers*, First Series (London : Macmillan & Co.), p. 52.

2 Barclay, *Brit. Med. Journ.*, 1912, vol. ii., p. 778.

3 Lauder Brunton, *Practitioner*, 1896, vol. lvii., p. 48.

4 Kocher, *Brit. Med. Journ.*, 1906, vol. i., p. 1266.

5 Lauder Brunton, *St Barth.'s Hosp. Journ.*, 1897, vol. v., p. 33.

6 Weir-Mitchell, *Fat and Blood*, 4th ed., 1885 (Philadelphia); Hale White, *Text-book of Pharmacology and Therapeutics*, 1901 (London): Pentland, p. 906.

7 For literature, *vide* Martius, *Tachycardie*, 1895 (Stuttgart); Hirschfelder, *Diseases of the Heart and Aorta*, 1910, p. 572.

8 Hirschfelder, *op. cit.*, 1910, p. 562.

9 A. Waller, *Practitioner*, 1870, vol. iv., p. 193 *et seq.*

10 Gibson and Ritchie, *Edin. Med. Journ.*, 1909, New Series, vol. ii., pp. 315 and 507.

11 Lauder Brunton, *Practitioner*, 1873, vol. xi., p. 246; reprinted in *Collected Papers*, First Series, p. 407.

12 *Ibid.*, p. 241; ibid., *Brit. Med. Journ.*, 1875, vol. ii., p. 695; and 1891, vol. ii., p. 1088.

[13] Lauder Brunton and others, *Brit Med. Journ.*, 1905, vol. ii., p. 1002.

[14] Lauder Brunton, *Practitioner*, 1888, vol. xl., p. 28.

[15] Cervello, *Arch. f. exp. Path. u. Pharm.*, 1883, Bd. xvi., p. 265; Bumke, *Münch. Med. Wochenschr.*, 1902, p. 1958.

[16] O. Liebreich, *Das Chloral, ein neues Hypnoticum und Anæstheticum*, 3te Aufl., 1871 (Berlin), p. 26; Hermann, *Lehrbuch d. exp. Toxikologie*, 1874 (Berlin), p. 271; Tomaszewicz, *Pflüger's Arch.*, 1874, Bd. ix., p. 35; Archangelsky, *Arch. f. exp. Path u. Pharm.*, 1901, Bd. xlvi., p. 347.

[17] Brunton and Stricker, *Journ. of Anat. and Physiol.*, 1874, vol. viii., p. 332; and *Collected Papers*, First Series, p. 197.

[18] Robert Jones, *Lancet*, 1913, vol. ii., p. 712; W. H. Willcox, *Brit. Med. Journ.*, 1913, vol. ii., p. 662.

[19] W. H. Willcox, *Brit. Med. Journ.*, 1913, vol. ii., p. 662.

[20] Kast, *Berl. Klin. Wochenschr.*, 1888, p. 309; Baumann and Kast, *Zeitschr. f. physiol. Chemie*, 1890, Bd. xiv., p. 52; Kast, *Arch. f. exp. Path. u. Pharm.*, 1893, Bd. xxxi., p. 69; see also Morro, *Deut. Med. Wochenschr.*, 1894, Nos. 34 and 30; Kobert, *Lehrbuch d. Intoxikationen*, 2te Aufl., 1906, Bd. ii., pp. 954-9.

[21] Schmiedeberg, *Arch. f. exp. Path. u. Pharm.*, 1886, Bd. xx., p. 203.

[22] Dreser, *Versamml. d. Naturforscher und Aerzte.*, 1899; E. Müller, *Münch. Med. Wochenschr.*, 1901, Nr. x., p. 383 (literature). See also *Brit. Med. Journ.* (Epit.), 1905, vol. i., p. 34; and *Brit. Med. Journ.*, 1909, vol. i., pp. 553-5.

[23] E. Fischer and v. Mering, *Therapie der Gegenwart*, 1904, vol. xlv., p. 97; Aug. Hofmann, *Inaug. Diss.*, Giessen, 1906; for recent literature, *vide* Martindale and Westcott, *Extra Pharmacopœia*, 1912, 15th ed., p. 778.

[24] *Pharmaceut. Zeitung*, 1910, p. 1029; Froehlich, *Brit. Med. Journ.* (Epit.), 1911, vol. i., p. 56; Kalischer, *ibid.*, 1911, vol. ii., p. 48.

[25] Cantlie, *Brit. Med. Journ.*, 1889, vol. i., p. 833.
[26] Voegtlin and Macht, *Journ. of Pharmacology and Exp. Therapeutics*, 1913, vol. v., p. 82.
[27] Lauder Brunton, *Lancet*, 1867, vol. ii., p. 97 ; *Reports of the Clinical Society*, 1870, vol. iii. ; reprinted in *Collected Papers*, First Series, pp. 137 and 185.
[28] D. J. Leech, *The Pharmacological Action and Therapeutical Uses of the Nitrites and allied Compounds*, 1902, pp. 113-6.
[29] Brunton and Tait, *St Barth.'s Hosp. Reports*, 1876, vol. xii., p. 144 ; reprinted in *Collected Papers*, First Series, p. 474 ; W. Murrell, *Lancet*, 1879, vol. i., pp. 80, 113, 151, 225 ; for full literature, *vide* D. J. Leech, *op. cit.*, p. 180.
[30] Bradbury, *Brit. Med. Journ.*, 1897, vol. i., p. 907. See also *Brit. Med. Journ.*, 1898, vol. i., pp. 18, 431 ; and 1899, vol. i., pp. 256, 1088 ; Russell, *Brit. Med. Journ.*, 1909, vol. ii., pp. 1110, 1314 ; Brunton, *Lancet*, 1908, vol. ii., p. 1132.
[31] Lauder Brunton, *International Clinics*, 1899, Eighth Series, vol. iii., p. 111 ; Huchard, *Maladies du Cœur et de l'Aorta*, 1899, 3me ed., vol. ii., p. 19.
[32] Lauder Brunton, *Practitioner*, 1905, p. 735.
[33] Lauder Brunton, *St Barth.'s Hosp. Reports*, 1883, vol. xix., p. 329.
[34] A. E. Wright, *Lancet*, 1897, vol. i., p. 303 ; Luff, *Brit. Med. Journ.*, 1909, vol. i., p. 261 ; Addis, *Brit. Med. Journ.*, 1909, vol. i., p. 999 (literature).
[35] Haig, *Diet and Food*, 4th ed. (London : Churchill), 1902.
[36] Oliver, *Blood and Blood-pressure*, 2nd ed., 1908, pp. 210-11 ; Barr, *Brit. Med. Journ.*, 1905, vol. i., p. 57.
[37] Lauder Brunton, *Clin. Soc. Reports*, vol. iii., 1870 ; reprinted in *Collected Papers*, First Series, p. 186.
[38] Lauder Brunton, *Lancet*, 1906, vol. ii., p. 1330 ; ibid., *Birmingham Medical Review*, 1909, vol. xiv., New Series, p. 191.
[39] A. E. Wright, *Brit. Med. Journ.*, 1891, vol. ii., p. 1306 ; 1893, vol. ii., p. 223 ; 1894, vol. i., p. 237, vol. ii., p. 57 ; *Lancet*, 1896, vol. i., p. 153, vol. ii., p. 807 ; 1897, vol. i., p. 303 ; 1905, vol. ii., p. 1096 ; Dixon,

Brit. Med. Journ., 1909, vol. ii., p. 540; Mayo Robson, *Lancet*, 1902, vol. i., p. 1024; Lauder Brunton, *Brit. Med. Journ.*, 1907, vol. i., p. 616; J. Barr, *Brit. Med. Journ.*, 1907, vol. i., p. 717; W. Blair Bell, *Brit. Med. Journ.*, 1907, vol. i., p. 920; Addis, *Brit. Med. Journ.*, 1909, vol. i., p. 997; Collingwood, *Brit. Med. Journ.*, 1910. vol. i., p. 507.

INDEX

NOTE: *In this Index the references to figures are to the pages on which they appear, and not to the numbers of the figures themselves.*

INDEX OF AUTHORS

NOTE: *The figures in italics refer to Literature at end of each chapter.*

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